

## Sequence Listing

Ashkenazi, Avi <110> Baker Kevin P. Botstein, David Desnoyers, Luc Eaton, Dan Ferrara, Napoleon Filvaroff, Ellen · Fong, Sherman Gao, Wei-Qiang Gerber, Hanspeter Gerritsen, Mary E. Goddard, Audrey Godowski, Paul J. Grimaldi, J. Christopher Gurney, Austin L. Hillan, Kenneth J Kljavin, Ivar J. Kuo, Sophia S. Napier, Mary A. Pan, James; Paoni, Nicholas F. Roy, Margaret Ann Shelton, David L. Stewart, Timothy A: Tumas, Daniel Williams, P. Mickey Wood, William I.

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| Asp  | Glu        | Ser   | Val   | Gly<br>125 | Ser  | Lys  | Thr  | Arg   | Arg<br>130 | Ala | Phe  | Leu  | Tyr  | Leu<br>135 |
| Ala  | Ala        | Phe   | Pro   | Phe<br>140 | Met  | Asp  | Ala  | Met   | Ala<br>145 | Trp | Thr  | His  |      | Gly<br>150 |
| Ile  | Leu        | Leu   | Lys   | His<br>155 | Lys  | Tyr  | Ser  | ' Phe | Leu<br>160 | Val | Gly  | Cys  | Ala  | Ser<br>165 |
| Ile  | Ser        | Asp   | Val   | Ile<br>170 | Ala  | Gln  | Val  | Val   | Phe<br>175 | Val | Ala  | Ile  | Leu  | Leu<br>180 |
| His  | Ser        | His   | Leu   | Glu<br>185 | Cys  | Arg  | Glu  | Pro   | Leu<br>190 | Leu | Ile  | Pro  | Ile  | Leu<br>195 |
| Ser  | Leu        | Tyr   | Met   | Gly<br>200 | Ala  | Leu  | Val  | Arg   | Cys<br>205 | Thr | Thr  | Leu  | Суз  | Leu<br>210 |

|   |   | Gly | Tyr   | Tyr | Lys  | Asn<br>215 | Ile | His | Asp | Ile  | Ile<br>220 | Pro | Asp | Arg | Ser | Gly<br>225  |     |   |   |           |   | , |   |
|---|---|-----|-------|-----|------|------------|-----|-----|-----|------|------------|-----|-----|-----|-----|-------------|-----|---|---|-----------|---|---|---|
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|   |   | Trp | Trp   | Pro | Leu  | Ala<br>245 | Leu | Ile | Leu | Ala  | Thr<br>250 | Gln | Arg | Ile | Ser | Arg<br>255  |     |   |   |           |   |   |   |
|   |   | Pro | Ile   | Val | Asn  | Leu<br>260 | Phe | Val | Ser | Arg  | Asp<br>265 | Leu | Gly | Gly | Ser | Ser<br>270  |     |   |   |           |   |   |   |
|   |   | Ala | Ala   | Thr | Glu  | Ala<br>275 | Val | Ala | Ile | Leu  | Thr<br>280 | Ala | Thr | Tyr | Pro | Val<br>285  |     |   |   |           |   |   |   |
|   |   | Gly | His   | Met | Pro  | Tyr<br>290 | Gly | Trp | Leu | Thr  | Glu<br>295 | Ile | Arg | Ala | Val | Tyr<br>300_ |     |   |   | · · · · · |   |   |   |
|   |   | Pro | Ala   | Phe | Asp  | Lys<br>305 | Asn | Asn | Pro | Ser  | Asn<br>310 | Lys | Leu | Val | Ser | Thr<br>315  |     |   |   |           |   |   |   |
|   |   | Ser | Asn   | Thr | Val  | Thr<br>320 | Ala | Ala | His | 'Ile | Lys<br>325 | Lys | Phe | Thr | Phe | Val<br>330  |     |   |   |           | • |   | ı |
|   |   | Cys | Met   | Ala | Leu  | Ser<br>335 | Leu | Thr | Leu | Cys  | Phe<br>340 | Val | Met | Phe | Trp | Thr<br>345  |     |   |   |           |   | · |   |
|   | · | Pro | Asn   | Val | Ser  | Glu<br>350 | Lys | Ile | Leu | Ile  | Asp<br>355 | Ile | Ile | Gly | Val | Asp<br>360  |     |   |   |           |   |   |   |
|   |   | Phe | Ala   | Phe |      | Glu<br>365 | Leu | Cys | Val | Val  | Pro<br>370 | Leu | Arg | Ile | Phe | Ser<br>375  |     |   |   |           | , |   |   |
|   |   | Phe | . Phe | Pro | Val  | Pro<br>380 | Val | Thr | Val | Arg  | Ala<br>385 | His | Leu | Thr | Gly | Trp<br>390  |     |   | - |           | • |   |   |
|   |   | Ľeu | Met   | Thr | Leu  | Lys<br>395 | Lys | Thr | Phe | Val  | Leu<br>400 | Ala | Pro | Ser | Ser | Val<br>405  | -   |   |   |           |   |   | • |
|   |   | Leu | Arg   | Ile | Ile  | Val<br>410 | Leu | Ile | Ala | Ser  | Leu<br>415 | Val | Val | Leu | Pro | Tyr<br>420  | . * |   |   |           |   | • |   |
|   | • | Leu | Gly   | Val | His' | Gly<br>425 | Ala | Thr | Leu | Gly  | Val<br>430 | Gly | Ser | Leu | Leu | Ala<br>435  |     | • | , |           |   |   |   |
|   |   | Gly | Phe   | Val | Gly  | Glu<br>440 | Ser | Thr | Met | Val  | Ala<br>445 | Ile | Ala | Ala | Cys | Tyr<br>450  |     |   |   |           |   |   | • |
|   |   | Val | Tyr   | Arg | Lys  | Gln<br>455 | Lys | Lys | Lys | Met  | Glu<br>460 | Asn | Glu | Ser | Ala | Thr<br>465  |     |   |   |           |   | , |   |
|   |   | Glu | Gly   | Glu | Asp  | Ser<br>470 | Ala | Met | Thr | Asp  | Met<br>475 | Pro | Pro | Thr | Glu | Glu<br>480  |     |   | : |           |   |   |   |
|   |   | Val | Thr   | Asp | Ile  | Val<br>485 | Glu | Met | Arg | Glu  | Glu<br>490 | Asn | Glu |     |     |             |     |   |   |           |   |   |   |
|   |   |     |       |     |      |            |     |     |     |      |            |     |     |     |     |             |     |   |   |           |   |   |   |
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Leu Phe Leu Gly Val Leu Val Ser Ile Ile Met Leu Ser Pro Gly

Val Glu Ser Gln Leu Tyr Lys Leu Pro Trp Val Cys Glu Glu Gly

Ala Gly Ile Pro Thr Val Leu Gln Gly His Ile Asp Cys Gly Ser

Leu Leu Gly Tyr Arg Ala Val Tyr Arg Met Cys Phe Ala Thr Ala

Ala Phe Phe Phe Phe Phe Thr Leu Leu Met Leu Cys Val Ser

Ser Ser Arg Asp Pro Arg Ala Ala Ile Gln Asn Gly Phe Trp Phe

Phe Lys Phe Leu Ile Leu Val Gly Leu Thr Val Gly Ala Phe Tyr

Ile Pro Asp Gly Ser Phe Thr Asn Ile Trp Phe Tyr Phe Gly Val 160

Val Gly Ser Phe Leu Phe Ile Leu Ile Gln Leu Val Leu Leu Ile 170 180

| Asp | Phe | Ala | His | Ser<br>185 | Trp  | Asn  | Gln | Arg | Trp<br>190 | Leu | Gly | Lys | Ala | Glu<br>195 |
|-----|-----|-----|-----|------------|------|------|-----|-----|------------|-----|-----|-----|-----|------------|
| Glu | Cys | Asp | Ser | Arg<br>200 | Ala  | Trp  | Tyr | Ala | Gly<br>205 | Leu | Phe | Phe | Phe | Thr<br>210 |
| Leu | Leu | Phe | Tyr | Leu<br>215 | Leu  | Ser  | Iļe | Ala | Ala<br>220 | Val | Ala | Leu | Met | Phe<br>225 |
| Met | Tyr | Tyr | Thr | Glu<br>230 | 'Pro | Ser  | Gly | Cys | His<br>235 | Glu | Gly | Lys | Val | Phe<br>240 |
| Ile | Ser | Leu | Asn | Leu<br>245 | Thr  | Phe  | Cys | Val | Cys<br>250 | Val | Ser | Ile | Ala | Ala<br>255 |
| Val | Leu | Pro | Lys | Val<br>260 | Gln  |      | Ala | Gln | Pro<br>265 | Asn | Ser | Gly | Leu | Leu<br>270 |
| Gln | Ala | Ser | Val | Ile<br>275 | Thr  | Leu  | Tyr | Thr | Met<br>280 | Phe | Val | Thr | Trp | Ser<br>285 |
| Ala | Leu | Ser | Ser | Ile<br>290 | Pro  | .Glu | Gln | Lys | Cys<br>295 | Asn | Pro | His | Leu | Pro<br>300 |
| Thr | Gln | Leu | Gly | Asn<br>305 | Glu  | Thr  | Val | Val | Ala<br>310 | Gly | Pro | Glu | Gly | Tyr<br>315 |
| Glu | Thr | Gln | Trp | Trp<br>320 | Asp  | Ala  | Pro | Ser | Ile<br>325 | Val | Gly | Leu | Ile | 330        |
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| Leu | Asp | Ala | Thr | Gln<br>365 | Gln  | Gln  | Gln | Gln | Gln<br>370 | Val | Ala | Ala | Cys | Glu<br>375 |
| Gly | Arg | Ala | Phe | Asp<br>380 | Asn  | Glu  | Gln | Asp | Gly<br>385 | Val | Thr | Tyr | Ser | Tyr<br>390 |
| Ser | Phe | Phe | His | Phe<br>395 | Cys  | Leu  | Val | Leu | Ala<br>400 | Ser | Leu | His | Val | Met<br>405 |
| Met | Thr | Leu | Thr | Asn<br>410 | Trp  | Tyr  | Lys | Pro | Gly<br>415 | Glu | Thr | Arg | Lys | Met<br>420 |
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Asp Ser Glu Val Leu Glu Glu Arg Gln Lys Arg Leu Pro Tyr Val 35 40 45

Pro Glu Pro Tyr Tyr Pro Glu Ser Gly Trp Asp Arg Leu Arg Glu 50 55 60

Leu Phe Gly Lys Asp Glu Gln Gln Arg Ile Ser Lys Asp Leu Ala  $\,$  65  $\,$   $\,$  70  $\,$  75

Asn Ile Cys Lys Thr Ala Ala Thr Ala Gly Ile Ile Gly Trp Val 80 85 90

Tyr Gly Gly Ile Pro Ala Phe Ile His Ala Lys Gln Gln Tyr Ile 95 100 105

Glu Gln Ser Gln Ala Glu Ile Tyr His Asn Arg Phe Asp Ala Val 110 115 120

Gln Ser Ala His Arg Ala Ala Thr Arg Gly Phe Ile Arg Tyr Gly
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130
137

Trp Arg Trp Gly Trp Arg Thr Ala Val Phe Val Thr Ile Phe Asn 140 145 150

Thr Val Asn Thr Ser Leu Asn Val Tyr Arg Asn Lys Asp Ala Leu 155 160 165

Ser His Phe Val Ile Ala Gly Ala Val Thr Gly Ser Leu Phe Arg 170 175 180

Ile Asn Val Gly Leu Arg Gly Leu Val Ala Gly Gly Ile Ile Gly
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Ala Leu Leu Gly Thr Pro Val Gly Gly Leu Leu Met Ala Phe Gln
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Lys Tyr Ala Gly Glu Thr Val Gln Glu Arg Lys Gln Lys Asp Arg

Lys Ala Leu His Glu Leu Lys Leu Glu Glu Trp Lys Gly Arg Leu 230 235 240

Gln Val Thr Glu His Leu Pro Glu Lys Ile Glu Ser Ser Leu Arg 245 250 255

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Phe Phe Tyr Met Ile Ile Leu Leu Leu Val Phe Ile Val Gln Phe

Ser Val Ser Cys Ala Cys Leu Ala Leu Asn Gln Glu Gln Gly

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                                  115
Asp Ile Gln Arg Asn Leu Asn Cys Cys Gly Phe Arg Ser Val Asn
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Pro Asn Asp Thr Cys Leu Ala Ser Cys Val Lys Ser Asp His Ser
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Cys Ser Pro Cys Ala Pro Ile Ile Gly Glu Tyr Ala Gly Glu Val
Leu Arg Phe Val Gly Gly Ile Gly Leu Phe Phe Ser Phe Thr Glu
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<212> DNA

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<213> Homo sapiens

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<223> Synthetic oligonucleotide probe

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Cys His Thr Glu Asp Asp Leu Thr Asp Ala Arg Glu Ala Gly Phe 50~ 55~ 60 60~

Gln Val Lys Ala Tyr Thr Phe Ser Glu Pro Phe His Leu Ile Val 65 70 75

Ser Tyr Asp Trp Leu Ile Leu Gln Gly Pro Ala Lys Pro Val Phe 80 85 90

Glu Gly Asp Leu Leu Val Leu Arg Cys Gln Ala Trp Gln Asp Trp 95 100 105

Pro Leu Thr Gln Val Thr Phe Tyr Arg Asp Gly Ser Ala Leu Gly 110 115 120

Pro Pro Gly Pro Asn Arg Glu Phe Ser Ile Thr Val Val Gln Lys 125 130 130

Ala Asp Ser Gly His Tyr His Cys Ser Gly Ile Phe Gln Ser Pro 140 145 150

Gly Pro Gly Ile Pro Glu Thr Ala Ser Val Val Ala Ile Thr Val 155 160 165

Gln Glu Leu Phe Pro Ala Pro Ile Leu Arg Ala Val Pro Ser Ala 170 175 180

Glu Pro Gln Ala Gly Ser Pro Met Thr Leu Ser Cys Gln Thr Lys 185 190 195

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<210> 52 <211> 321 <212> PRT <213> Homo sapiens

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Leu Gln Gly Tyr Thr Gln Val Leu Val Lys Trp Leu Val Gln Arg
50 55 60

Gly Ser Asp Pro Val Thr Ile Phe Leu Arg Asp Ser Ser Gly Asp
65 70 75

His Ile Gln Gln Ala Lys Tyr Gln Gly Arg Leu His Val Ser His 80 85 90

Lys Val Pro Gly Asp Val Ser Leu Gln Leu Ser Thr Leu Glu Met 95 100 105

Asp Asp Arg Ser His Tyr Thr Cys Glu Val Thr Trp Gln Thr Pro 110 115 120

Asp Gly Asn Gln Val Val Arg Asp Lys Ile Thr Glu Leu Arg Val 125 130 135

Gln Lys Leu Ser Val Ser Lys Pro Thr Val Thr Gly Ser Gly 140 145 150

Tyr Gly Phe Thr Val Pro Gln Gly Met Arg Ile Ser Leu Gln Cys 155 160 165

Gln Ala Arg Gly Ser Pro Pro Ile Ser Tyr Ile Trp Tyr Lys Gln
170 175 180

Gln Thr Asn Asn Gln Glu Pro Ile Lys Val Ala Thr Leu Ser Thr 185 190 195

200 205 Cys Thr Ala Lys Gly Gln Val Gly Ser Glu Gln His Ser Asp Ile 220 215 Val Lys Phe Val Val Lys Asp Ser Ser Lys Leu Leu Lys Thr Lys 235 Thr Glu Ala Pro Thr Thr Met Thr Tyr Pro Leu Lys Ala Thr Ser 250 Thr Val Lys Gln Ser Trp Asp Trp Thr Thr Asp Met Asp Gly Tyr 265 Leu Gly Glu Thr Ser Ala Gly Pro Gly Lys Ser Leu Pro Val Phe 280 275 Ala Ile Ile Leu Ile Ile Ser Leu Cys Cys Met Val Val Phe Thr 290 Met Ala Tyr Ile Met Leu Cys Arg Lys Thr Ser Gln Gln Glu His 310 305 Val Tyr Glu Ala Ala Arg 320 <210> 53 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 53 tatccctcca attgagcacc ctgg 24 <210> 54 <211> 21 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 54 gtcggaagac atcccaacaa g 21 <210> 55 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe

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<211> 373

<212> PRT

<213> Homo sapiens

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Val Thr Leu Pro Cys His His Gln Leu Gly Leu Pro Glu Lys Asp 35 40 45

Thr Leu Asp Ile Glu Trp Leu Leu Thr Asp Asn Glu Gly Asn Gln 50 55 60

Lys Val Val Ile Thr Tyr Ser Ser Arg His Val Tyr Asn Asn Leu 65 70 75

Thr Glu Glu Gln Lys Gly Arg Val Ala Phe Ala Ser Asn Phe Leu 80 85 90

Ala Gly Asp Ala Ser Leu Gln Ile Glu Pro Leu Lys Pro Ser Asp 95 100 105

Glu Gly Arg Tyr Thr Cys Lys Val Lys Asn Ser Gly Arg Tyr Val 110 115 120

Trp Ser His Val Ile Leu Lys Val Leu Val Arg Pro Ser Lys Pro 125 130 135

Lys Cys Glu Leu Glu Gly Glu Leu Thr Glu Gly Ser Asp Leu Thr 140 145 150

Leu Gln Cys Glu Ser Ser Ser Gly Thr Glu Pro Ile Val Tyr Tyr 155 160 165

Trp Gln Arg Ile Arg Glu Lys Glu Gly Glu Asp Glu Arg Leu Pro

Gly Asn Glu Ala Gly Lys Glu Ser Cys Val Val Arg Val Thr Val 215 220 225

Gln Tyr Val Gln Ser Ile Gly Met Val Ala Gly Ala Val Thr Gly 230 235 240

Ile Val Ala Gly Ala Leu Leu Ile Phe Leu Leu Val Trp Leu Leu 245 250 255

Ile Arg Arg Lys Asp Lys Glu Arg Tyr Glu Glu Glu Glu Arg Pro 260 265 270

Asn Glu Ile Arg Glu Asp Ala Glu Ala Pro Lys Ala Arg Leu Val 275 280 285

Lys Pro Ser Ser Ser Ser Ser Gly Ser Arg Ser Ser Arg Ser Gly
290 295 300

Ser Ser Ser Thr Arg Ser Thr Ala Asn Ser Ala Ser Arg Ser Gln 305 310 315

Arg Thr Leu Ser Thr Asp Ala Ala Pro Gln Pro Gly Leu Ala Thr 320 325 330

Gln Ala Tyr Ser Leu Val Gly Pro Glu Val Arg Gly Ser Glu Pro 335 \$340

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<sup>&</sup>lt;210> 64

<sup>&</sup>lt;211> 655

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|          |     |     |     |            |      |     |       |       |            |     |      |       |     |            |     |      | • |  |
|----------|-----|-----|-----|------------|------|-----|-------|-------|------------|-----|------|-------|-----|------------|-----|------|---|--|
| Met<br>1 | Gly | Thr | Ser | Pro<br>5   | Ser  | Ser | Ser   | Thr   | Ala<br>10  | Leu | Ala  | Ser   | Cys | Ser<br>15  |     |      |   |  |
| Arg      | Ile | Ala | Arg | Arg<br>20  | Ala  | Thr | Ala   | Thr   | Met<br>25  | Ile | Ala  | Gly   | Ser | Leu<br>30  |     |      | • |  |
| Leu      | Leu | Leu | Gly | Phe<br>35  | .Leu | Ser | Thr   | Thr   | Thr<br>40  | Ala | Gln  | Pro   | Glu | Gln<br>45  |     |      |   |  |
| Lys      | Ala | Ser | Asn | Leu<br>.50 | Ile  | Gly | Thr   | Tyr   | Arg<br>55  | His | Val  | Asp   | Arg | Ala<br>60  |     |      |   |  |
| Thr      | Gly | Gln | Val | Leu<br>65. |      | Cys | Asp   | Lys   | Cys<br>70  | Pro | Ala  | Gly   | Thr | Tyr<br>75  |     |      |   |  |
| <br>Val  | Ser | Glu | His | Cys<br>_80 | Thr  | Asn | Thr   |       | Leu<br>85  |     | Val  | Cys   | Ser | Ser<br>90  | - / | <br> |   |  |
| Cys      | Pro | Val | Gly | Thr<br>95  | Phe  | Thr | Arg   | His   | Glu<br>100 | Asn | Gly  | Ile   | Glu | Lys<br>105 |     |      |   |  |
| Cys      | His | Asp | Cys | Ser<br>110 | Gln  | Pro | Cys   | Pro   | Trp<br>115 | Pro | Met  | Ile   | Glu | Lys<br>120 |     |      |   |  |
| Leu      | Pro | Cys | Ala | Ala<br>125 | Leu  | Thr | Asp   | Arg   | Glu<br>130 | Cys | Thr  | Cys   | Pro | Pro<br>135 |     |      |   |  |
| Gly      | Met | Phe | Gln | Ser<br>140 | Asn  | Ala | Thr   | Cys   | Ala<br>145 | Pro | His  | Thr   | Val | Cys<br>150 |     |      |   |  |
| Pro      | Val | Gly | Trp | Gly<br>155 | Val  | Arg | Lys   | Lys   | Gly<br>160 | Thr | Glu  | Thr   | Glu | Asp<br>165 |     |      | ` |  |
| Val      | Arg | Cys | Lys | Gln<br>170 | Cys  | Ala | Arg   | Gly   | Thr<br>175 |     | Ser  | Asp   | Val | Pro<br>180 |     |      |   |  |
| Ser      | Ser | Val | Met | Lys<br>185 | Cys  | Lys | Ala   | Tyr   | Thr<br>190 |     | Cys  | Leu   | Ser | Gln<br>195 |     |      |   |  |
| Asn      | Leu | Val | Val | 11e<br>200 |      | Pro | Gly   | Thr   | Lys<br>205 |     | .Thr | Asp   | Asn | Val<br>210 |     |      |   |  |
| Cys      | Gly | Thr | Leu | Pro<br>215 |      | Phe | Ser   | Ser   | Ser<br>220 |     | Ser  | . Pro | Ser | Pro<br>225 |     |      |   |  |
| Gly      | Thr | Ala | Ile | Phe<br>230 |      | Arg | Pro   | Glu   | His<br>235 |     | Glu  | Thr   | His | Glu<br>240 |     |      |   |  |
| Val      | Pro | Ser | Ser | Thr<br>245 |      | Val | Pro   | Lys   | Gly<br>250 |     | Asn  | Ser   | Thr | Glu<br>255 |     |      |   |  |
| Ser      | Asn | Ser | Ser | Ala<br>260 |      | Val | . Arg | y Pro | 265        |     | Leu  | Ser   | Ser | 1le<br>270 |     |      |   |  |
| Gln      | Glu | Gly | Thr | Val<br>275 |      | Asp | Asr   | n Thr | Ser<br>280 |     | Ala  | Arg   | Gly | Lys<br>285 |     |      |   |  |

|   | Glu | Asp | Val | Asn | Lys<br>290 | Thr | Leu | Pro | Asn | Leu<br>295 | GIn | Val | vaı | Asn | 300        |   |      |                    |    |        |
|---|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|---|------|--------------------|----|--------|
|   | Gln | Gln | Gly | Pro | His<br>305 | His | Arg | His | Ile | Leu<br>310 | Lys | Leu | Leu | Pro | Ser<br>315 |   |      |                    |    |        |
|   | Met | Glu | Ala | Thr | Gly<br>320 | Gly | Glu | Lys | Ser | Ser<br>325 | Thr | Pro | Ile | Lys | Gly<br>330 |   |      | •                  |    |        |
|   | Pro | Lys | Arg | Gly | His<br>335 | Pro | Arg | Gln | Asn | Leu<br>340 | His | Lys | His | Phe | Asp<br>345 |   |      |                    |    |        |
|   | Ile | Asn | Glu | His | Leu<br>350 | Pro | Trp | Met | Ile | Val<br>355 | Leu | Phe | Leu | Leu | Leu<br>360 |   |      |                    |    |        |
|   | Val | Leu | Val | Val | Ile<br>365 | Val | Val | Суз | Ser | Ile<br>370 | Arg | Lys | Ser | Ser | Arg<br>375 |   | <br> | <del>-</del> - · - |    |        |
|   | Thr | Leu | Lys | Lys | Gly<br>380 | Pro | Arg | Gln | Asp | Pro<br>385 | Ser | Ala | Ile | Val | Glu<br>390 |   | ٠.   |                    |    | · . ·. |
|   | Lys | Ala | Gly | Leu | Lys<br>395 | Lys | Ser | Met | Thr | Pro<br>400 | Thr | Gln | Asn | Arg | Glu<br>405 |   |      |                    |    |        |
|   | Lys | Trp | Ile | Tyr | Tyr<br>410 | Cys | Asn | Gly | His | Gly<br>415 | Ile | Asp | Ile | Leu | Lys<br>420 | • |      |                    |    | •      |
|   | Leu | Val | Ala | Ala | Gln<br>425 | Val | Gly | Ser | Gln | Trp<br>430 |     | Asp | Ile | Tyr | Gln<br>435 |   |      |                    | ٠. | •      |
|   | Phe | Leu | Cys | Asn | Ala<br>440 | Ser | Glu | Arg | Glu | Val<br>445 |     | Ala | Phe | Ser | Asn<br>450 |   |      |                    |    |        |
|   | Gly | Tyr | Thr | Ala | Asp<br>455 | His | Glu | Arg | Ala | Tyr<br>460 |     | Ala | Leu | Gln | His<br>465 |   |      |                    |    |        |
|   | Trp | Thr | Ile | Arg | Gly<br>470 | Pro | Glu | Ala | Ser | Leu<br>475 |     | Gln | Leu | Ile | Ser<br>480 |   |      |                    | -  |        |
|   | Ala | Leu | Arg | Gln | His<br>485 | Arg | Arg | Asn | Asp | Val<br>490 |     | Glu | Lys | Ile | Arg<br>495 |   |      |                    |    |        |
|   | Gly | Leu | Met |     | Asp<br>500 |     |     |     |     |            | Thr |     |     |     | Ala<br>510 |   |      |                    |    |        |
|   | Leu | Pro | Met | Ser | Pro<br>515 | Ser | Pro | Leu | Ser | Pro<br>520 |     | Pro | Ile | Pro | Ser<br>525 |   |      |                    |    |        |
|   | Pro | Asn | Ala | Lys | Leu<br>530 |     | Asn | Ser | Ala | Leu<br>535 |     | Thr | Val | Glu | Pro<br>540 |   |      |                    |    |        |
|   | Ser | Pro | Gln | Asp | Lys<br>545 | Asn | Lys | Gly | Phe | Phe<br>550 |     | Asp | Glu | Ser | Glu<br>555 |   |      |                    |    |        |
|   | Pro | Leu | Leu | Arg | Cys<br>560 |     | Ser | Thr | Ser | Ser<br>565 |     | Ser | Ser | Ala | Leu<br>570 |   |      |                    |    |        |
|   |     |     |     |     |            |     |     |     |     |            |     |     | •   |     |            |   |      |                    |    |        |
| ı |     |     |     |     |            |     |     |     |     |            |     |     |     |     |            |   |      |                    |    |        |
|   |     |     |     |     |            |     |     |     |     |            |     |     |     |     |            |   |      |                    |    |        |

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Asp Asp Met Leu His Phe Leu Asn Pro Glu Glu Leu Arg Val Ile
               605
                               610
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<212> DNA
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Pro Asp Ala Asp Ala Val Ala Ala Gln Ile Leu Ser Leu Leu Pro 35 40 45

Leu Lys Phe Phe Pro Ile Ile Val Ile Gly Ile Ile Ala Leu Ile

<sup>&</sup>lt;211> 453

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

| Leu | Ala<br>~ | Leu | Ala  | Ile<br>65  | Gly | Leu | Gly   | Ile | His<br>70  | Phe | Asp | Cys | Ser  | Gly<br>75  |  |
|-----|----------|-----|------|------------|-----|-----|-------|-----|------------|-----|-----|-----|------|------------|--|
| Lys | Tyr      | Arg | Cys  | Arg<br>80  | Ser | Ser | Phe   | Lys | Cys<br>85  | Ile | Glu | Leu | Ile  | Ala<br>90  |  |
| Arg | Cys      | Asp | Gly  | Val<br>95  | Ser | Asp | Cys   | Lys | Asp<br>100 | Gly | Glu | Asp | Glu  | Tyr<br>105 |  |
| Arg | Cys      | Val | Arg  | Val<br>110 | Gly | Gly | Gln   | Asn | Ala<br>115 | Val | Leu | Gln | Val  | Phe<br>120 |  |
| Thr | Ala      | Ala | Ser  | Trp<br>125 | r , | Thr | Met   | Cys | Ser<br>130 |     | Asp | Trp | Lys  | Gly<br>135 |  |
| His | -Tyr-    | Ala | -Asn | Val<br>140 | Ala | Cys | -Al'a | Gln | Leu<br>145 | Gly | Phe | Pro | Ser  | Tyr<br>150 |  |
| Val | Ser      | Ser | Asp  | Asn<br>155 | Leu | Arg | Val   | Ser | Ser<br>160 | Leu | Glu | Gly | Gl'n | Phe<br>165 |  |
| Arg | Glu      | Glu | Phe  | Val<br>170 | Ser | Ile | Asp   | His | Leu<br>175 | Leu | Pro | Asp | Asp  | Lys<br>180 |  |
| Val | Thr      | Ala | Leu  | His<br>185 | His | Ser | Val   | Tyr | Val<br>190 | Arg | Glu | Gly | Cys  | Ala<br>195 |  |
| Ser | Gly.     | His | Val  | Val<br>200 | Thr | Leu | Gln   | Cys | Thr<br>205 | Ala | Cys | Gly | His  | Arg<br>210 |  |
| Arg | Gly      | Tyr | Ser  | Ser<br>215 | Arg | Ile | Val   | Gly | Gly<br>220 | Asn | Met | Ser | Leu  | Leu<br>225 |  |
| Ser | Gln      | Trp | Pro  | Trp<br>230 | Gln | Ala | Ser   | Leu | Gln<br>235 | Phe | Gln | Gly | Tyr  | His<br>240 |  |
| Leu | Cys      | Gly | Gly  | Ser<br>245 | Val | Ile | Thr   | Pro | Leu<br>250 | Trp | Ile | Ile | Thr  | Ala<br>255 |  |
| Ala | His      | Cys | Val  | Tyr<br>260 | Asp | Leu | Tyr   | Leu | Pro<br>265 | Lys | Ser | Trp | Thr  | Ile<br>270 |  |
| Gln | Val      | Gly | Leu  | Val<br>275 | Ser | Leu | Leu   | Asp | Asn<br>280 | Pro | Ala | Pro | Ser  | His<br>285 |  |
| Leu | Val      | Glu | Lys  | Ile<br>290 | Val | Tyr | His   | Ser | Lys<br>295 | Tyr | Lys | Pro | Lys  | Arg<br>300 |  |
| Leu | Gly      | Asn | Asp  | 11e<br>305 | Ala | Leu | Met   | Lys | Leu<br>310 | Ala | Gly | Pro | Leu  | Thr<br>315 |  |
| Phe | Asn      | Glu | Met  | Ile<br>320 | Gln | Pro | Val   | Cys | Leu<br>325 | Pro | Asn | Ser | Glu  | Glu<br>330 |  |
| Asn | Phe      | Pro | Asp  | Gly        | Lys | Val | Cys   | Trp | Thir       | Ser | Gly | Trp | Gly  | Ala        |  |

Thr Glu Asp Gly Gly Asp Ala Ser Pro Val Leu Asn His Ala Ala 350 355 360

Val Pro Leu Ile Ser Asn Lys Ile Cys Asn His Arg Asp Val Tyr 365 370 375

Gly Gly Ile Ile Ser Pro Ser Met Leu Cys Ala Gly Tyr Leu Thr 380 385 390

Gly Gly Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val 395 400 405

Cys Gln Glu Arg Arg Leu Trp Lys Leu Val Gly Ala Thr Ser Phe 410 415 420

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Val Ser Leu Trp Asn Gln Gly Arg Ala Asp Glu Val Val Ser Ala 35 40 45

Ser Val Arg Ser Gly Asp Leu Trp Ile Pro Val Lys Ser Phe Asp 50 55 60

Ser Lys Asn His Pro Glu Val Leu Asn Ile Arg Leu Gln Arg Glu 65 70 75

Ser Lys Glu Leu Ile Ile Asn Leu Glu Arg Asn Glu Gly Leu Ile 80 85 90

Ala Ser Ser Phe Thr Glu Thr His Tyr Leu Gln Asp Gly Thr Asp 95 100 105

Val Ser Leu Ala Arg Asn Tyr Thr Gly His Cys Tyr Tyr His Gly 110 115 120

|   | His | Val | Arg | Gly     | Tyr<br>125 | Ser | Asp | Ser | Ala | Val<br>130  | Ser | Leu | Ser | Thr | Cys<br>135 |              |   |      |     |
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|   | Ser | Gly | Leu | Arg     | Gly<br>140 | Leu | Ile | Val | Phe | Glu<br>145  | Àsn | Glu | Ser | Tyr | Val<br>150 |              |   |      |     |
|   | Leu | Glu | Pro | Met     | Lys<br>155 | Ser | Ala | Thr | Asn | Arg<br>160  | Tyr | Lys | Leu | Phe | Pro<br>165 |              |   |      |     |
|   | Ala | Lys | Lys | Leu     | Lys<br>170 | Ser | Val | Arg | Gly | Ser<br>175  | Cys | Gly | Ser | His | His<br>180 |              |   |      |     |
|   | Asn | Thr | Pro | Asn     | Leu<br>185 | Ala | Ala | Lys | Asn | Val<br>190  | Phe | Pro | Pro | Pro | Ser<br>195 |              |   |      |     |
|   | Gln | Thr | Trp | Ala<br> | Arg<br>200 | Arg |     | _   | -   | Glu<br>-205 |     |     | Lys |     | Thr<br>210 | rado de rado | - | <br> | . 8 |
|   | Lys | Tyr | Val | Glu     | Leu<br>215 | Val | Ile | Val | Ala | Asp<br>220  | Asn | Arg | Glu | Phe | Gln<br>225 |              |   | •    |     |
|   | Arg | Gln | Gly | Lys     | Asp<br>230 | Leu | Glu | Lys | Val | Lys<br>235  | Gln | Arg | Leu | Ile | Glu<br>240 |              |   |      | į.  |
|   | Ilė | Ala | Asn | His     | Val<br>245 | Asp | Lys | Phe | Tyr | Arg<br>250  | Pro | Leu | Asn | Ile | Arg<br>255 |              |   |      |     |
|   | Ile | Val | Leu | Val     | Gly<br>260 | Val | Glu | Val | Trp | Asn<br>265  | Asp | Met | Asp | Lys | Cys<br>270 |              | , |      |     |
|   | Ser | Val | Ser | Gln     | Asp<br>275 | Pro | Phe | Thr | Ser | Leu<br>280  | His | Glu | Phe | Leu | Asp<br>285 |              |   |      |     |
|   | Trp | Arg | Lys | Met     | Lys<br>290 | Leu | Leu | Pro | Arg | Lys<br>295  | Ser | His | Asp | Asn | Ala<br>300 |              |   |      |     |
|   | Gln | Leu | Val | Ser     | Gly<br>305 | Val | Tyr | Phe | Gln | Gly<br>310  | Thr | Thr | Ile | Gly | Met<br>315 |              |   |      |     |
| • | Ala | Pro | Ile | Met     | Ser<br>320 | Met | Cys | Thr | Ala | Asp<br>325  | Gln | Ser | Gly | Gly | Ile<br>330 | ÷            |   |      |     |
|   | Val | Met | Asp | His     | Ser<br>335 | Asp | Asn | Pro | Leu | Gly<br>340  |     | Ala | Val | Thr | Leu<br>345 | ·            |   |      |     |
|   | Ala | His | Glu | Leu     | Gly<br>350 | His | Asn | Phe | Gly | Met<br>355  | Asn | His | Asp | Thr | Leu<br>360 | •            |   |      |     |
|   | Asp | Arg | Gly | Cys     | Ser<br>365 |     | Gln | Met | Ala | Val<br>370  |     | Lys | Gly | Gly | Cys<br>375 |              |   |      |     |
|   | Ile | Met | Asn | Ala     | Ser<br>380 | Thr | Gly | Tyr | Pro | Phe<br>385  |     | Met | Val | Phe | Ser<br>390 |              |   |      |     |
|   | Ser | Cys | Ser | Arg     | Lys<br>395 | Asp | Leu | Glu | Thr | Ser<br>400  |     | Glu | Lys | Gly | Met<br>405 |              |   |      |     |
|   |     |     |     |         |            |     |     |     |     |             |     |     |     |     |            |              |   |      |     |
|   |     |     |     |         |            |     |     |     |     |             |     |     |     |     |            |              |   |      |     |

|   | GIÀ     | vaı     | Cys | Leu | 410        | ASN | Leu | PIO | GIU | 415         | AIG | GIU      | ser | rne   | 420          |      |             |   |      |   |
|---|---------|---------|-----|-----|------------|-----|-----|-----|-----|-------------|-----|----------|-----|-------|--------------|------|-------------|---|------|---|
|   | Gly     | Gln     | Lys | Cys | Gly<br>425 | Asn | Arg | Phe | Val | Glu<br>430  | Glu | Gly      | Glu | Glu   | Cys<br>435   |      |             |   |      |   |
|   | Asp     | Cys     | Gly | Glu | Pro<br>440 | Glu | Glu | Cys | Met | Asn<br>445  | Arg | Суѕ      | Cys | Asn   | Ala<br>450   |      |             |   |      |   |
|   | Thr     | Thr     | Cys | Thr | Leu<br>455 | Lys | Pro | Asp | Ala | Val<br>460  | Cys | Ala<br>, | His | Gly   | Leu<br>465   |      |             |   |      |   |
|   | Cys     | Cys     | Glu | Asp | Cys<br>470 | Gln | Leu | Lys | Pro | Ala<br>475  | Gly | Thr      | Ala | Cys   | Arg<br>480   |      |             |   |      |   |
|   | Asp<br> | Ser<br> | Ser | Asn | Ser<br>485 |     |     |     |     | Glu<br>-490 |     | Cys      | Thr | Gly   | Ala<br>'4'95 | <br> | ·. <u>-</u> |   | <br> | - |
|   | Ser     | Pro     | His | Cys | Pro<br>500 | Ala | Asn | Val | Tyr | Leu<br>505  | His | Asp      | Gly | His   | Ser<br>510   |      |             |   |      |   |
|   | Cys     | Gln     | Asp | Val | Asp<br>515 | Gly | Tyr | Суѕ | Tyr | Asn<br>520  | Gly | Ile      | Cys | Gln   | Thr<br>525   |      |             |   |      |   |
| • | His     | Glu     | Gln | Gln | Cys<br>530 |     | Thr | Leu | Trp | Gly<br>535  | Pro | Gly      | Ala | Lys   | Pro<br>540   |      |             |   | ٠.   |   |
|   | Aļla    | Pro     | Gly | Ile | Cys<br>545 | Phe | Glu | Arg | Val | Asn<br>550  | Ser | Ala      | Gly | Asp   | Pro<br>555   | •    |             | • |      |   |
|   | Tyr     | Gly     | Asn | Суз | Gly<br>560 | Lys | Val | Ser | Lys | Ser<br>565  | Ser | Phe      | Ala | Lys   | Cys<br>570   |      |             |   |      |   |
|   | Glu     | Met     | Arg | Asp | Ala<br>575 | Lys | Cys | Gly | Lys | Ile<br>580  |     | Cys      | Gln | Gly   | Gly<br>585   |      |             | • |      |   |
|   | Ala     | Ser     | Arg | Pro | Val<br>590 |     | Gly | Thr | Asn | Ala<br>595  |     | Ser      | Ile | Glu   | Thr<br>600   |      |             |   |      |   |
|   | Asn     | Ile     | Pro | Leu | Gln<br>605 | Gln | Gly | Gly | Arg | Ile<br>610  |     | Cys      | Arg | Gly   | Thr<br>615   |      |             |   |      |   |
|   | His     | Val     | Tyr | Leu | Gly<br>620 | Asp | Asp | Met | Pro | Asp<br>625  |     | Gly      | Leu | Val   | Leu<br>.630  |      |             |   | `    |   |
|   | Ala     | Gly     | Thr | Lys | Cys<br>635 |     | Asp | Gly | Lys | Ile<br>640  |     | Leu      | Asn | Arg   | Gln<br>645   |      |             |   |      |   |
|   | Cys     | Gln     | Asn | Ile | Ser<br>650 |     | Phe | Gly | Val | His<br>655  |     | Cys      | Ala | Met   | Gln<br>660   |      |             |   |      |   |
|   | Cys     | His     | Gly | Arg | Gly<br>665 |     | Cys | Asn | Asn | Arg<br>670  |     | Asn      | Cys | His   | Cys<br>675   |      |             | • | •    |   |
|   | Glu     | Ala     | His | Trp | Ala<br>680 |     | Pro | Phe | Cys | Asp<br>685  |     | Phe      | Gly | , Phe | Gly<br>690   |      |             |   |      |   |

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20 25 30

Gly Gly Arg Trp Gly Ala Arg Ala Gln Glu Ala Ala Ala Ala Ala 45

|      |           |            |      |      |     |       |        |      |      |       |            |      | •     |        |      | `  |   |
|------|-----------|------------|------|------|-----|-------|--------|------|------|-------|------------|------|-------|--------|------|--|---|
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      |           |            |      |      |     | •     |        |      |      |       |            |      |       |        |      |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      | • .                                      |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      | Ala       | Asp        | Gly  | Pro  | Pro | Ala   | Ala    | Asp  | Gly  | Glu   | Asp        | Gly  | Gln   | Asp    | Pro  |  |   |
|      |           | _          | _    |      | 50  |       |        | _    |      | 55    | -          | _    |       | -      | 60   |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      | *  |   |
|      | His       | Ser        | Lys  | His  | Leu | Tyr   | Thr    | Ala  | Asp  | Met   | Phe        | Thr  | His   | Gly    | Ile  | •  |   |
|      |           |            | _    |      | 65  |       |        |      | _    | 70    |            |      |       | _      | 75   |  |   |
|      |           | •          |      |      |     |       | •      |      |      |       |            |      |       |        |      |  |   |
|      | Gln       | Ser        | Ala  | Ala  | His | Phe   | Val    | Met  | Phe  | Phe   | Ala        | Pro  | Trp   | Cys    | Gly  |  |   |
|      |           |            |      |      | 80  |       |        |      |      | 85    |            |      | ٠.    |        | 90   | · · · · · · · · · · · · · · · · · · ·    |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      | His       | Cys        | Gln  | Arg  | Leu | Gln   | Pro    | Thr  | Trp  | Asn   | Asp        | Leu  | Gly   | Asp    | Lys  |  |   |
|      |           |            |      |      | 95  |       | •      |      |      | 100   |            |      |       |        | 105  | •  |   |
|      |           |            |      |      |     |       | _      |      |      |       |            |      |       |        |      |  |   |
|      | Tyr       | Asn        | Ser  | Met  | Glu | Asp   | Ala    | Lys  | Val  |       | Val        | Ala  | Lys   | Val    | Asp  |  |   |
|      |           |            |      |      | 110 |       |        |      |      | 115   |            |      |       |        | 120  |  |   |
|      | _         |            |      |      |     |       |        |      |      | . 130 |            |      |       | ٠.     |      | *  |   |
|      | Cys       | Thr        | Ala  |      | Ser |       | Val    | Cys  | Ser  |       |            | Gly  | Val   | Arg    |      |  | _ |
|      |           |            |      | :    | 125 |       |        |      |      | 130   |            |      |       |        | 135  |  |   |
|      | _         | <u>.</u>   |      |      | _   |       |        |      |      |       |            |      |       |        | _    |  |   |
|      | Tyr       | Pro        | Thr  | Leu  | Lys | Leu   | Phe    | Lys  | Pro  |       | Gln        | Glu  | Ala   | Val    | _    | •  |   |
|      |           |            |      |      | 140 |       | :      |      |      | 145   |            |      |       |        | 150  |  |   |
| •    | _         | -          | ۵,   | _    | _   |       |        |      |      | _     | ~ .        | _    | _     |        |      | ·  |   |
|      | Tyr       | GĻn        | GLy  | Pro  | Arg | Asp   | Phe    | GIn  | Thr  |       |            | Asn  | Trp   | Met    |      |  |   |
|      |           |            |      |      | 155 |       |        |      |      | 160   |            |      |       | ٠.     | 165. | *  |   |
|      | 0.1       | m1         |      |      |     | 0.1   | _      |      | m)   | _     | <b>~</b> 1 | _    | -     |        |      | v en |   |
|      | GIN       | Thr        | Leu  | Asn  | Glu | GLu   | Pro    | vaı  | Thr  |       | GLu        | Pro  | Glu   | Val    |      |  |   |
|      |           |            |      |      | 170 |       |        |      |      | 175   |            |      |       |        | 180  |  |   |
|      | ,<br>D=== | Dwa        | Com  | 71-  | Dwa | C1    | T 0.12 | T    | C1-  | C1    | T 0        | m    | C1    | T      | Cam  |  |   |
|      | PIO       | PIO        | ser  | Ald  | Pro | GIU   | ьеи    | гуѕ  | GIII |       |            | ıyı  | GIU   | Leu    |      |  |   |
|      |           |            |      |      | 185 |       |        |      |      | 190   |            |      |       |        | 195  |  |   |
|      | 71-       | C 0 x      | 700  | Dho  | Glu | T 011 | ш. с   | 17-1 | 71-  | Cln   | C1         | 7.00 | u i o | Dho    | T10  | **                                       |   |
|      | ura.      | 261        | ASII | FILE | 200 | Dea   | 1113   | Val  | AIA  | 205   | GLY        | hsp  | птэ   | . File | 210  | *  |   |
|      |           |            |      |      | 200 |       |        |      |      | 203   |            |      |       |        | 210  |  |   |
|      | Lve       | Phe        | Pho  | Δla  | Prò | Trn   | Cvs    | Glv  | His  | Cvs   | T.vs       | Δla  | T.011 | Δla    | Pro  |  |   |
|      | Lys,      | 1110       | 1110 | ALG  | 215 | TIP   | Cys    | OLY  | 1113 | 220   | БуЗ        | nια  | пси   | NJ.C   | 225  |  |   |
|      |           |            |      | - 1. | 213 |       |        |      |      | 220   |            |      |       | ٠.     | 223  |  |   |
|      | Thr       | Tro        | Glu  | Gln  | Len | Ala   | Len    | Glv  | Leu  | Glu   | His        | Ser  | Gĺu   | Thr    | Val  |  |   |
| •    |           |            | 0.10 | 01   | 230 |       |        | .023 | 200  | 235   |            | 001  |       |        | 240  | •  |   |
|      | •         |            | •    |      | 200 |       |        |      |      |       |            |      |       |        | 2.0  |  |   |
|      | Lvs       | Ile        | ·Glv | Lvs  | Vaĺ | Asp   | Cvs    | Thr  | Gln  | His   | Tvr        | Glu  | Leu   | Cvs    | Ser  |  |   |
|      |           |            | 1    | -1-  | 245 |       | -,,-   |      |      | 250   |            |      |       | -,-    | 255  |  |   |
|      | ,         |            |      |      |     |       |        |      |      |       |            |      |       |        | 7:   | α ÷ ×                                    |   |
|      | Glv       | Asn        | Gln  | Val  | Arg | Gly   | Tyr    | Pro  | Thr  | Leu   | Leu        | Trp  | Phe   | Arq    | Asp  | *  |   |
|      | _         |            |      |      | 260 |       | -      |      |      | 265   |            | •    |       |        | 270  |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      | •  |   |
|      | Gly       | Lys        | Lys  | Val  | Asp | Gln   | Tyr    | Lys  | Gly  | Lys   | Arg        | Asp  | Leu   | Glu    | Ser  |  |   |
|      | _         | <u>-</u> . | •    |      | 275 |       | _      | -    |      | 280   |            | -    | · · · |        | 285  |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      | Leu       | Arg        | Glu  | Tyr  | Val | Glu   | Ser    | Gln  | Leu  | Gln   | Arg        | Thr  | Glu   | Thr    | Gly  |  |   |
| 2.23 |           |            |      |      | 290 |       |        |      |      | 295   |            |      |       |        | 300  |  |   |
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|      | Ala       | Thr        | Glu  | Thr  | Val | Thr   | Pro    | Ser  | Glu  | Ala   | Pro        | Val  | Leu   | Ala    | Ala  |  |   |
|      |           |            |      |      | 305 |       |        |      |      | 310   |            |      |       |        | 315  |  |   |
|      |           |            |      |      | •   |       |        |      |      |       |            |      |       |        |      |  |   |
| ·    | Glu       | Pro        | Glu  | Ala  | Asp | Lys   | Gly    | Thr  | Val  | Leu   | Ala        | Leu  | . Thr | Glu    | Asn  |  |   |
|      |           |            |      |      | 320 | •     |        | •    |      | 325   |            |      | **    |        | 330  |  |   |
|      |           |            |      |      | •   |       |        |      |      |       |            |      |       |        |      | • • •                                    |   |
|      |           |            |      |      |     |       |        |      |      |       |            | • •  | ٦.    |        |      | •  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      | ·  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      | •  |   |
|      |           |            |      |      |     |       |        |      |      |       |            |      |       |        |      |  |   |

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Glu Glu Leu Ser Lys Lys Glu Phe Pro Gly Leu Ala Gly Val Lys
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Tyr Ser Val Arg Gly Tyr Pro Thr Leu Leu Leu Phe Arg Gly Gly
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Lys Lys Val Ser Glu His Ser Gly Gly Arg Asp Leu Asp Ser Leu
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Asp Ser Arg Pro Thr Ala Glu Val Cys Ala Thr His Thr Ile Ser 35 40 45

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Glu Gly Lys His Gly Lys Val Gly Arg Met Gly Pro Lys Gly Ile 65 70 75

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Thr Gly Pro Ile Gly Lys Lys Gly Asp Lys Gly Glu Lys Gly Leu 95 100 105

Leu Gly Ile Pro Gly Glu Lys Gly Lys Ala Gly Thr Val Cys Asp 110 115 120

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Gly Met Leu Ala Met Pro Lys Asp Glu Ala Ala Asn Thr Leu Ile 185 190 195

Ala Asp Tyr Val Ala Lys Ser Gly Phe Phe Arg Val Phe Ile Gly

200 205 210

Val Asn Asp Leu Glu Arg Glu Gly Gln Tyr Met Ser Thr Asp Asn 215 220 225

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<213> Homo sapiens

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Gln Leu Glu Arg Ala Ala Leu Gly Phe Arg Lys Gly Gly Ser Gly
20 25 30

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|---|-----|----------|-----|-----|--------------|-----|-----|----------|-----|------------------------|-----|-----|-----|-----|-------------|----------|
|   |     |          |     |     |              |     |     |          |     |                        |     |     |     |     |             |          |
|   | Met | Phe      | Ala | Ser | Gly<br>35    | Trp | Asn | Gln      | Thr | Val <sup>-</sup><br>40 | Pro | Ile | Glu | Glu | Ala<br>45   |          |
|   | Gly | Ser      | Met | Ala | Ala<br>50    | Leu | Leu | Leu      | Leu | Pro<br>55              | Leu | Leu | Leu | Leu | Leu<br>60   |          |
|   | Pro | Leu      | Leu | Leu | Leu<br>65    | Lys | Leu | His      | Leu | Trp<br>70              | Pro | Gln | Leu | Arg | Trp<br>75   | ,        |
|   | Leu | Pro      | Ala | Asp | Leu<br>80    | Ala | Phe | Ala      | Val | Arg<br>85              | Ala | Leu | Cys | Cys | Lys<br>90   |          |
|   | Arg | Ala      | Leu | Arg | Ala<br>95    | Arg | Ala | Leu      | Ala | Ala<br>100             | Ala | Ala | Ala | Asp | Pro<br>105  | •        |
|   | Glu | Gly<br>- | Pro |     | Gly<br>-110- |     |     | Ser<br>- |     | Ala<br>-115            |     | Arg | Leu | Ala | Glu<br>120- | <u> </u> |
|   | Leu | Ala      | Gln | Gln | Arg<br>125   | Ala | Ala | His      | Thr | Phe<br>130             | Leu | Ile | His | Gly | Ser<br>135  |          |
|   | Arg | Arg      | Phe | Ser | Tyr<br>140   | Ser | Glu | Ala      | Glu | Arg<br>145             | Glu | Ser | Asn | Arg | Ala<br>150  |          |
|   | Ala | Arg      | Ala | Phe | Leu<br>155   | Arg | Ala | Leu      | Gly | Trp<br>160             | Asp | Trp | Gly | Pro | Asp<br>165  |          |
|   | Gly | Gly      | Asp | Ser | Gly<br>170   | Glu | Gly | Ser      | Ala | Gly<br>175             | Glu | Gly | Glu | Arg | Ala<br>180  |          |
|   | Ala | Pro      | Gly | Ala | Gly<br>185   | Asp | Ala | Ala      | Ala | Gly<br>190             |     | Gly | Ala | Glu | Phe<br>195  |          |
|   | Ala | Gly      | Gly | Asp | Gly<br>200   | Ala | Ala | Arg      | Gly | Gly<br>205             |     | Ala | Ala | Ala | Pro<br>210  |          |
|   | Leu | Ser      | Pro | Gly | Ala<br>215   | Thr | Val | Ala      | Leu | Leu<br>220             | Leu | Pro | Ala | Gly | Pro<br>225  |          |
|   | Glu | Phe      | Leu | Trp | Leu<br>230   | Trp | Phe | Gly      | Leu | Ala<br>235             |     | Ala | Gly | Leu | Arg<br>240  |          |
|   | Thr | Ala      | Phe | Val | Pro<br>245   |     | Ala | Leu      | Arg | Arg<br>250             |     | Pro | Leu | Leu | His<br>255  |          |
|   | Cys | Leu      | Arg | Ser | Cys<br>260   | Gly | Ala | Arg      | Ala | Leu<br>265             |     | Leu | Ala | Pro | Glu<br>270  |          |
|   |     |          |     |     | 275          |     |     |          |     | 280                    |     |     |     |     | Met<br>285  |          |
|   |     |          |     |     | 290          |     |     |          |     | 295                    |     |     |     |     | Gly<br>300  |          |
|   | Ile | Ser      | Asp | Leu | Leu<br>305   |     | Glu | Val      | Ser | Ala<br>310             |     | Val | Asp | Gly | Pro<br>315  |          |
|   |     |          |     |     |              |     |     |          |     |                        |     |     |     |     |             |          |
|   |     |          |     |     |              | •   |     |          |     |                        | ,   |     |     |     |             |          |
|   |     |          |     |     |              |     |     |          |     |                        |     |     |     |     |             |          |

|   | Val  | Pro | Gly | Tyr | Leu<br>320 | Ser | Ser      | Pro  | Gln | Ser<br>325 | Ile | Thr | Asp  | Thr | Cys<br>330 |    |    |   |        |              |
|---|------|-----|-----|-----|------------|-----|----------|------|-----|------------|-----|-----|------|-----|------------|----|----|---|--------|--------------|
|   | Leu  | Tyr | Ile | Phe | Thr<br>335 | Ser | Gly      | Thr  | Thr | Gly<br>340 | Leu | Pro | Lys  | Ala | Ala<br>345 |    | ٠  |   |        |              |
|   | Arg  | Ile | Ser | His | Leu<br>350 | Lys | Ile      | Leu  | Gln | Cys<br>355 | Gln | Gly | Phe  | Tyr | Gln<br>360 |    |    | • |        |              |
|   | Leu  | Cys | Gly | Val | His<br>365 | Gln | Glu      | Asp  | Val | Ile<br>370 | Tyr | Leu | Ala  | Leu | Pro<br>375 |    |    |   |        |              |
|   | Leu  | Tyr | His | Met | Ser<br>380 | Gly | Ser      | Leu  | Leu | Gly<br>385 | Ile | Val | Gly  | Cys | Met<br>390 |    |    |   |        |              |
|   | Gly  | Ile | Gly |     | Thr<br>395 |     |          |      | Lys |            | _   |     |      | Ala |            |    |    |   | <br>   | <del>-</del> |
|   | Gln  | Phe | Trp | Glu | Asp<br>410 | Cys | Gln      | Gl'n | His | Arg<br>415 | Val | Thr | `Val | Phe | Gln<br>420 |    |    | • |        |              |
|   | Tyr  | Ile | Gly | Glu | Leu<br>425 | Cys | Arg      | Tyr  | Leu | Val<br>430 | Asn | Gln | Pro  | Pro | Ser<br>435 |    |    |   |        |              |
|   | Lys. | Ala | Glu | Arg | Gly<br>440 | His | Lys      | Val  | Arg | Leu<br>445 | Ala | Val | Gly  | Ser | Gly<br>450 |    |    |   |        |              |
|   | Leu  | Arg | Pro | Asp | Thr        | Trp | Glu      | Arg  | Phe | Val<br>460 | Arg | Arg | Phe  | Gly | Pro<br>465 |    |    |   |        | ٠            |
|   | Leu  | Gln | Val | Leu | Glu<br>470 | Thr | Tyr      | Gly  | Leu | Thr<br>475 | Glu | Gly | Àsn  | Val | Ala<br>480 |    |    |   |        | ,            |
|   | Thr  | Ile | Asn | Tyr | Thr<br>485 | Gly | Gln      | Arg  | Gly | Ala<br>490 | Val | Gly | Arg  | Ala | Ser<br>495 |    |    |   | ,      |              |
|   | Trp  | Leu | Tyr | Lys | His<br>500 | Ile | Phe      | Pro  | Phe | Ser<br>505 | Leu | Ile | Arg  | Tyr | Asp<br>510 | *  | •  | • |        |              |
| * | Val  | Thr | Thr | Gly | Glu<br>515 | Pro | Ile      | Arg  | Asp | Pro<br>520 | Gln | Gly | His  | Cys | Met<br>525 |    |    |   | <br>8, |              |
|   | Ala  | Thr | Ser | Pro | Gly<br>530 | Glu | Pro      | Gly  | Leu | Leu<br>535 | Val | Ala | Pro  | Val | Ser<br>540 |    | ·ž |   |        |              |
|   | Gln  | Gln | Ser | Pro | Phe<br>545 | Leu | Gly      | Tyr  | Ala | Gly<br>550 | _   | Pro | Glu  | Leu | Ala<br>555 | ٠. |    |   |        |              |
|   | Gln  | Gly | Lys | Leu | Leu<br>560 | Lys | Asp      | Val  | Phe | Arg<br>565 | Pro | Gly | Asp  | Val | Phe<br>570 |    |    |   |        |              |
|   | Phe  | Asn | Thr | Gly | Asp<br>575 | Leu | Leu<br>· | Val  | Cys | Asp<br>580 |     | Gln | Gly  | Phe | Leu<br>585 |    |    |   |        |              |
|   | Arg  | Phe | His | Asp | Arg<br>590 | Thr | Gly      | Asp  | Thr | Phe<br>595 |     | Trp | Lys  | Gly | Glu<br>600 |    |    |   |        |              |

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Phe Leu Gln Glu Val Asn Val Tyr Gly Val Thr Val Pro Gly His
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Glu Gly Arg Ala Gly Met Ala Ala Leu Val Leu Arg Pro Pro His
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Pro Pro Tyr Ala Arg Pro Arg Phe Leu Arg Leu Gln Glu Ser Leu
Ala Thr Thr Glu Thr Phe Lys Gln Gln Lys Val Arg Met Ala Asn
 Glu Gly Phe Asp Pro Ser Thr Leu Ser Asp Pro Leu Tyr Val Leu
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 cttggggctg ctgctctccc tccccgccgg ggcggatgtg aaggctcgga 650
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Gly Glu Val Arg Gln Ala Tyr Gly Ala Lys Gly Phe Ser Leu Ala 35 40 45

Asp Ile Pro Tyr Gln Glu Ile Ala Gly Glu His Leu Arg Ile Cys 50 55 60

Pro Gln Glu Tyr Thr Cys Cys Thr Thr Glu Met Glu Asp Lys Leu 65 70 75

Ser Gln Gln Ser Lys Leu Glu Phe Glu Asn Leu Val Glu Glu Thr  $80 \ \ 85 \ \ 90$ 

Ser His Phe Val Arg Thr Thr Phe Val Ser Arg His Lys Lys Phe 95 100 105

Asp Glu Phe Phe Arg Glu Leu Leu Glu Asn Ala Glu Lys Ser Leu 110 115 120

Asn Asp Met Phe Val Arg Thr Tyr Gly Met Leu Tyr Met Gln Asn 125 130 135

Ser Glu Val Phe Gln Asp Leu Phe Thr Glu Leu Lys Arg Tyr Tyr 140 145 150

| 1111 | GIÀ | GIY | ASII | 155        | ASII             | pea | GIU              |     | 160        | ьeu | ASII | изр | 1116 | 165        |
|------|-----|-----|------|------------|------------------|-----|------------------|-----|------------|-----|------|-----|------|------------|
| Ala  | Arg | Leu | Leu  | Glu<br>170 | Arg              | Met | Phe              | Gln | Leu<br>175 | Ile | Asn  | Pro | Gln  | Tyr<br>180 |
| His  | Phe | Ser | Glu  | Asp<br>185 | Tyr              | Leu | Glu              | Cys | Val<br>190 | Ser | Lys  | Tyr | Thr  | Asp<br>195 |
| Gln  | Leu | Lys | Pro  | Phe<br>200 | Gly              | Asp | Val              | Pro | Arg<br>205 | Lys | Leu  | Lys | Ile  | Gln<br>210 |
| Val  | Thr | Arg | Ala  | Phe<br>215 | Ile              | Ala | Ala              | Arg | Thr<br>220 | Phe | Val  | Gln | Gly  | Leu<br>225 |
| Thr  |     |     | Arg  |            |                  |     |                  |     |            |     | Lys  | Val |      | Pro<br>240 |
| Thr  | Pro | Gly | Cys  | Ile<br>245 | Arg <sup>:</sup> | Ala | Leu              | Met | Lys<br>250 | Met | Leu  | Tyr | Cys  | Pro<br>255 |
| Tyr  | Cys | Arg | Gly  | Leu<br>260 | Pro              | Thr | Val-             | Arg | Pro<br>265 | Cys | Asn  | Asn | Tyr  | Cys<br>270 |
| Leu, | Asn | Val | Met  | Lys<br>275 | Gly              | Cys | Leu              | Ala | Asn<br>280 | Gln | Ala  | Asp |      | Asp<br>285 |
| Thr  | Glu | Trp | Asn  | Leu<br>290 | Phe              | Ile | Asp              | Ala | Met<br>295 | Leu | Leu  | Val | Ala  | Glu<br>300 |
| Arg  | Leu | Glu | Gly  | Pro<br>305 | Phe              | Asn | lle              | Glu | Ser<br>310 | Val | Met  | Asp | Pro  | Ile<br>315 |
| Asp  | Val | Lys | Ile  | Ser<br>320 | Glu              | Ala | Ile              | Met | Asn<br>325 | Met | Gln  | Glu | Asn  | Ser<br>330 |
| Met  | Gln | Val | Ser  | Ala<br>335 | Lys              | Val | Phe <sub>,</sub> | Gln | Gly<br>340 | Cys | Gly  | Gln | Pro  | Lys<br>345 |
| Pro  | Ala | Pro | Ala  | Leu<br>350 | Arg              | Ser | Ala              | Arg | Ser<br>355 | Ala | Pro  | Glu | Asn  | Phe<br>360 |
| Asn  | Thr | Arg | Phe  | Arg<br>365 |                  | Tyr | Asn              | Pro | Glu<br>370 | Glu | Arg  | Pro | Thr  | Thr<br>375 |
| Ala  | Ala | Gly | Thr  | Ser<br>380 |                  | Asp | Arg              | Leu | Val<br>385 | Thr | Asp  | Ile | Lys  | Glu<br>390 |
| Lys  | Leu | Lys | Leu  | Ser<br>395 | Lys              | Lys | Val              | Trp | Ser<br>400 | Ala | Leu  | Pro | Tyr  | Thr<br>405 |
| Ile  | Cys | Lys | Asp  | Glu<br>410 | Ser              | Val | Thr              |     | Gly<br>415 | Thr | Ser  | Asn | Glu  | Glu<br>420 |
| Glu  | Cys | Trp | Asn  | Gly<br>425 | His              | Ser | Lys              | Ala | Arg<br>430 | Tyr | Leu  | Pro | Glu  | Ile<br>435 |

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Val Asp Ile Thr Arg Pro Asp Thr Phe Ile Arg Gln Gln Ile Met
               455
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Asn Asp Val Asn Phe Gln Asp Thr Ser Asp Glu Ser Ser Gly Ser
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                                  490
Gly Ser Gly Ser Gly Cys Met Asp Asp Val Cys Pro Thr Glu Phe
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Ala Gly Phe Trp Ile Leu Cys Leu Leu Thr Tyr Gly Tyr Leu Ser 35 40 45

Trp Gly Gln Ala Leu Glu Glu Glu Glu Glu Gly Ala Leu Leu Ala 50 55 60

Gln Ala Gly Glu Lys Leu Glu Pro Ser Thr Thr Ser Thr Ser Gln
65 70 75

Pro His Leu Ile Phe Ile Leu Ala Asp Asp Gln Gly Phe Arg Asp 80 85 90

Val Gly Tyr His Gly Ser Glu Ile Lys Thr Pro Thr Leu Asp Lys 95 100 105

Leu Ala Ala Glu Gly Val Lys Leu Glu Asn Tyr Tyr Val Gln Pro 110 115 120

Ile Cys Thr Pro Ser Arg Ser Gln Phe Ile Thr Gly Lys Tyr Gln
125 130 135

Ile His Thr Gly Leu Gln His Ser Ile Ile Arg Pro Thr Gln Pro 140 145 150

<sup>&</sup>lt;210> 114

<sup>&</sup>lt;211> 515

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|   | Asn | Cys | Leu | Pro | Leu<br>155 | Asp      | Asn | Ala | Thr | Leu <sup>.</sup><br>160 | Pro | Gln | Lys | Leu | Lys<br>165 |   |              |   |            |     |  |
|---|-----|-----|-----|-----|------------|----------|-----|-----|-----|-------------------------|-----|-----|-----|-----|------------|---|--------------|---|------------|-----|--|
|   | Glu | Val | Gly | Tyr | Ser<br>170 | Thr      | His | Met | Val | Gly<br>175              | Lys | Trp | His | Leu | Gly<br>180 |   |              |   |            |     |  |
|   | Phe | Asn | Arg | Lys | Glu<br>185 | Cys      | Met | Pro | Thr | Arg<br>190              | Arg | Gly | Phe | Asp | Thr<br>195 |   |              |   |            |     |  |
|   | Phe | Phe | Gly | Ser | Leu<br>200 | Leu      | Gly | Ser | Gly | Asp<br>205              | Tyŗ | Tyr | Thr | His | Tyr<br>210 |   | •            |   |            |     |  |
|   | Lys | Cys | Asp | Ser | Pro<br>215 | Gly      | Met | Cys | Gly | Tyr<br>220              | Asp | Leu | Tyr | Glu | Asn<br>225 |   |              |   |            |     |  |
|   | Asp | Asn | Ala |     |            | Asp      |     |     |     |                         |     | Tyr | Ser | Thr | Gln<br>240 |   | <del>-</del> |   | <b>.</b> . |     |  |
|   | Met | Tyr | Thr | Gln | Arg<br>245 | Val      | Gln | Gln | Ile | Leu<br>250              | Ala | Ser | His | Àsn | Pro<br>255 |   |              |   |            |     |  |
| • | Thr | Lys | Pro | Ile | Phe<br>260 | Leu      | Ťyr | Thr | Ala | Tyr<br>265              | Gln | Ala | Val | His | Ser<br>270 |   |              |   |            | *   |  |
|   | Pro | Leu | Gln | Ala | Pro<br>275 | Gly      | Arg | Tyr | Phe | Glu<br>280              | His | Tyr | Arg | Ser | Ile<br>285 | • |              |   |            |     |  |
|   | Ile | Asn | Ile | Asn | Arg<br>290 | Arg      | Arg | Tyr | Ala | Ala<br>295              | Met | Leu | Ser | Cys | Leu<br>300 |   |              |   |            |     |  |
|   | Asp | Glu | Ala | Ile | Asn<br>305 | Aşn      | Val | Thr | Leu | Ala<br>310              | Leu | Lys | Thr | Tyr | Gly<br>315 |   |              |   |            |     |  |
|   | Phe | Tyr | Asn | Asn | Ser<br>320 | .,Ile    | Ile | Ile | Tyr | Ser<br>325              | Ser | Asp | Asn | Gly | Gly<br>330 |   | •            | į |            |     |  |
|   | Gln | Pro | Thr | Ala | Gly<br>335 | Gly      | Ser | Asn | Trp | Pro<br>340              |     | Arg | Gly | Ser | Lys<br>345 |   |              |   |            |     |  |
|   | Gly | Thr | Tyr | Trp | Glu<br>350 | Gly<br>· | Gly | Ile | Arg | Ala<br>355              |     | Gly | Phe | Val | His<br>360 |   |              | , |            |     |  |
| • | Ser | Pro | Leu | Leu | Lys<br>365 | Asn      | Lys | Gly | Thr | Val<br>370              |     | Lys | Glu | Leu | Val<br>375 |   |              | * |            | 8 . |  |
|   | His | Ile | Thr | Asp | Trp<br>380 | Tyr      | Pro | Thr | Leu | Ile<br>385              |     | Leu | Ala | Glu | Gly<br>390 |   |              |   |            | ,   |  |
|   | Gln | Ile | Asp | Glu | Asp<br>395 | Ile      | Gln | Leu | Asp | Gly<br>400              |     | Asp | Ile | Trp | Glu<br>405 |   |              |   | •          |     |  |
|   | Thr | Ile | Ser | Glu | Gly<br>410 | Leu      | Arg | Ser | Pro | Arg<br>415              |     | Asp | Ile | Leu | His<br>420 |   |              |   |            |     |  |
|   | Asn | Ile | Asp | Pro | Tyr<br>425 | Thr      | Pro | Arg | Gln | Lys<br>430              |     | Ala | Pro | Gly | Gln<br>435 |   |              |   |            |     |  |

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Gln Ala Met Gly Ser Gly Thr Leu Gln Ser Ser Gln Pro Ser Glu
                440
                                   445
Cys Ser Thr Gly Asn Cys Leu Gln Glu Ile Leu Ala Thr Ala Thr
                                    460
                455
Gly Ser Pro Leu Ser Leu Ser Ala Thr Trp Asp Arg Thr Gly Gly
                                   475
 Thr Met Asn Gly Ser Pro Cys Gln Leu Ala Lys Val Tyr Gly Phe
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                485
 Ser Thr Ser Gln Pro Thr His Met Arg Gly Trp Thr Tyr Leu Thr
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 Gly Ile Gln Glu Ser
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<211> 338

<212> PRT

<213> Homo sapiens

<400> 119

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|      | Val | Ala | Gly | Gly  | Phe<br>20  | Gly | Asn | Ala | Ala | Ser<br>25  | Ala | Arg      | His | His   | Gly<br>30  |   |           |     |   |  |
|------|-----|-----|-----|------|------------|-----|-----|-----|-----|------------|-----|----------|-----|-------|------------|---|-----------|-----|---|--|
|      | Leu | Leu | Ala | Ser- | Ala<br>35  | Arg | Gln | Pro | Gly | Val<br>40  | Cys | His      | Tyr | Gly   | Thr<br>45  |   |           |     |   |  |
|      | Lys | Leu | Ala | Cys  | Cys<br>50  | Tyr | Gly | Trp | Arg | Arg<br>55  | Asn | Ser      | Lys | Gly   | Val<br>60  |   |           |     |   |  |
| , it | Суѕ | Glu | Ala | Thr  | Cys<br>65  | Glu | Pro | Gly | Cys | Lys<br>70  | Phe | Gly      | Glu | Cys   | Val<br>75  |   |           |     |   |  |
|      | Gly | Pro | Asn | Lys  | Cys<br>80  | Arg | Cys | Phe | Pro | Gly<br>85  | Tyr | Thr      | Ģly | Lys   | Thr<br>90  |   |           |     | • |  |
|      | Cys | Ser | Gln | Asp  | Val<br>95  | Asn | Glu | Суѕ | Gly | Met<br>100 | Lys | Pro      | Arg | Pro   | Cys<br>105 |   |           |     |   |  |
|      | Gln | His | Arg | Cys  | Val<br>110 | Asn | Thr | His | Gly | Ser<br>115 | Tyr | Lys      | Cys | Phe   | Cys<br>120 | = | <br>· · · |     |   |  |
|      | Leu | Ser | Gly | His  | Met<br>125 | Leu | Met | Pro | Asp | Ala<br>130 | Thr | Cys      | Val | Asn   | Ser<br>135 |   |           |     |   |  |
|      | Arg | Thr | Cys | Ala  | Met<br>140 | Ile | Asn | Cys | Gln | Tyr<br>145 | Ser | Cys      | Glu | Asp   | Thr<br>150 |   |           |     |   |  |
|      | Glu | Glu | Gly | Pro  | Gln<br>155 | Cys | Leu | Cys | Pro | Ser<br>160 |     | Gly      | Leu | Arg   | Leu<br>165 |   |           |     |   |  |
|      | Ala | Pro | Asn | Gly  | Arg<br>170 |     | Cys | Leu | Asp | Ile<br>175 |     | Glu      | Cys | Ala   | Ser<br>180 |   |           |     |   |  |
|      | Gly | Lys | Val | Ile  | Cys<br>185 |     | Tyr | Asn | Arg | Arg<br>190 |     | Val      | Asn | Thr   | Phe<br>195 |   |           |     |   |  |
|      | Gly | Ser | Tyr | Tyr  | Cys<br>200 | -   | Cys | His | Ile | Gly<br>205 |     | Glu      | Leu | Gln   | Tyr<br>210 |   |           | . 8 |   |  |
|      | Ile | Ser | Gly | Arg  | Tyr<br>215 | _   | Cys | Ile | Asp | Ile<br>220 |     | Glu      | Cys | Thr   | Met<br>225 |   |           | •   |   |  |
|      | Asp | Ser | His | Thr  | Cys<br>230 |     | His | His | Ala | Asn<br>235 |     | Phe      | Asn | Thr   | Gln<br>240 |   |           |     |   |  |
| •    | Gly | Ser | Phe | Lys  | Cys<br>245 |     | Cys | Lys | Gln | Gly<br>250 |     | Lys      | Gly | Asn   | Gly<br>255 |   |           |     |   |  |
|      | Leu | Arg | Cys | Ser  | Ala<br>260 |     | Pro | Glu | Asn | Ser<br>265 |     | Lys<br>· | Glu | Val   | Leu<br>270 |   |           |     |   |  |
|      | Arg | Ala | Pro | Gly  | Thr<br>275 |     | Lys | Asp | Arg | Ile<br>280 | -   | Lys      | Leu | . Leu | Ala<br>285 |   |           |     |   |  |
|      | His | Lys | Asn | Ser  | Met<br>290 |     | Lys | Lys | Ala | Lys<br>295 |     | Lys      | Asr | . Val | Thr<br>300 |   |           |     |   |  |

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<210> 124

<211> 289.

<212> PRT

<213> Homo sapiens

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Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu 35 40 45

Glu Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu
50 55 60

|   | Asp   | Leu  | Thr | Asp | Thr<br>65  | Gly | Ser | His | Glu | Ala<br>70  | Ala | Thr | Lys | Ala | Val<br>75  |
|---|-------|------|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|
|   | Leu   | Gln  | Glu | Phe | Gly<br>80  | Arg | Ile | Asp | Ile | Leu<br>85  | Val | Asn | Asn | Gly | Gly<br>90  |
|   | Met   | Ser  | Gln | Arg | Ser<br>95  | Leu | Cys | Met | Asp | Thr<br>100 | Ser | Leu | Asp | Val | Tyr<br>105 |
|   | Arg   | Lys  | Leu | Ile | Glu<br>110 | Leu | Asn | Tyr | Leu | Gly<br>115 | Thr | Val | Ser | Leu | Thr<br>120 |
|   | Lys   | Cys  | Val | Leu | Pro<br>125 | His | Met | Ile | Glu | Arg<br>130 | Lys | Gln | Gly | Lys | Ile<br>135 |
|   | Val   | Thr  | Val | Asn | Ser<br>140 |     | Leu | _   | Ile | Ile<br>145 | Ser | Val | Pro | Leu | Ser<br>150 |
|   | Ile   | Gly  | Tyr | Cys | Ala<br>155 | Ser | Lys | His | Ala | Leu<br>160 | Arg | Gly | Phe | Phe | Asn<br>165 |
|   | Gly   | Leu  | Arg | Thr | Glu<br>170 | Leu | Ala | Thr | Tyr | Pro<br>175 | Gly | Ile | Ile | Val | Ser<br>180 |
|   | Asn   | Ile  | Cys | Pro | Gly<br>185 | Pro | Val | Gln | Ser | Asn<br>190 | Ile | Val | Glu | Asn | Ser<br>195 |
|   | Leu   | Ala  | Gly | Glu | Val<br>200 | Thr | Lys | Thr | Ile | Gly<br>205 | Asn | Asn | Gly | Asp | Gln<br>210 |
|   | Ser   | His  | Lys | Met | Thr<br>215 | Thr | Ser | Arg | Cys | Val<br>220 | Arg | Leu | Met | Leu | Ile<br>225 |
|   | Ser   | Met  | Ala | Asn | Asp<br>230 | Leu | Lys | Glu | Val | Trp<br>235 | Ile | Ser | Glu | Gln | Pro<br>240 |
|   | Phe   | Leu  | Leu | Val | Thr<br>245 | Tyr | Leu | Trp | Gln | Tyr<br>250 | Met | Pro | Thr | Trp | Ala<br>255 |
|   | Trp   | Trp  | Ile | Thr | Asn<br>260 | Lys | Met | Gly | Lys | Lys<br>265 | Arg | Ile | Glu | Asn | Phe<br>270 |
|   | Lys   | Ser  | Gly | Val | Asp<br>275 | Ala | Asp | Ser | Ser | Tyr<br>280 |     | Lys | Ile | Phe | Lys<br>285 |
|   | Thr   | Lys  | His | Asp |            |     | ı   |     |     |            |     |     |     |     |            |
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|-----|---|------|-------|------|------|------------|-------------|------|------|---------|------------|-------|------|------|-------|------------|-------|
|     |   | T1 - | mi    | m)   |      |            | <b>71</b> - | 7    | 17-1 | C       | T          | Mat   | m    | Tou  | 202   | Dho        |       |
|     |   | TIE  | Thr   | Tnr  | Tyr  | A1a<br>35  | TTE         | Asn  | vai  | ser     | 40.        | мет   | Trp  | Leu  | ser   | 45         | 4.    |
|     |   | λνα  | Tuc   | Wa I | Gln  | Clu        | Pro         | Gln  | Glv  | Luc     | Δla        | T.ve  | Ara  | His  | Glv   | Δsn        |       |
|     |   | nry  | цуз   | Vai  | GIII | 50         | FIO         | GIII | GIY  | цуз     | 55         |       | nrg  |      | Oly   | . 60       |       |
| •   |   | Thr  | Val   | Pro  | Gly  | Glu        | Trp         | Pro  | Trp  | Gln     | Ala        | Ser   | Val  | Arg  | Arg   | Gln        |       |
|     |   |      |       |      |      | 65         |             |      |      |         | 70         |       |      |      |       | 75         |       |
|     |   | Gly  | Ala   | His  | Ile  | Cys        | Ser         | Gly  | Ser  | Leu     | Val        | Ala   | Asp  | Thr  | Trp   | Val        |       |
| ,   |   |      |       |      |      | 80         | ,           |      |      |         | 85         |       |      |      |       | 90         |       |
| ,   |   | Leu  | Thṛ   | Ala  | Ala  |            | Cys         | Phe  | Glu  | Lys     |            | Ala   | Ala  | Thr  | Glu   |            |       |
| •   |   |      |       |      |      | 95         |             |      |      | •       | 100        |       |      |      |       | 105        |       |
| . • |   | Asn  | Ser   | Trp  | Ser  |            | Val         | Leu  | Gly  | Ser     |            | Gln   | Arg  | Glu  | Gly   |            | i igi |
|     |   |      | · :   |      |      | 110        |             |      |      | - :- :  | 115        |       |      |      |       | 120        |       |
|     |   | Ser  | Pro   | Gly  | Ala  | Glu<br>125 | Glu         | Val  | Gly  | Val     | Ala<br>130 | Ala   | Leu  | Gln  | Leu   | Pro        |       |
|     |   |      |       |      |      |            |             |      |      |         |            | •     |      |      | •     |            |       |
|     | ` | Arg  | Ala   | Tyr  | Asn  | His<br>140 | Tyr         | Ser  | Gln  | Gly     | Ser        |       | Leu  | Ala  | Leu   | Leu<br>150 |       |
|     |   |      |       |      | ** * |            | m)          | m)   | 11 d | mb      |            |       | C    | T a  | Dwa   | ·,<br>Cln  |       |
| . ~ |   | GIN  | Leu   | Ala  | His  | 155        |             | Tnr  | нiг  | Thr     | 160        | Leu   | Cys  | reu  | PIO   | 165        |       |
|     |   | Pro  | Δ1 =  | Hic  | Arg  | Dha        | Pro         | Pho  | Glv  | Δla     | Ser        | Cvs.  | Trn  | Ala  | Thr   | Glv        |       |
|     |   |      | AIG   | 1113 | nrg  | 170        |             | THE  | Cly  | nia     | 175        | Oyb   | 110  |      | *     | 180        |       |
|     | • | Trp  | Asp   | Gln  | Asp  | Thr        | Ser         | Asp  | Ala  | Pro     | Glv.       | Thr   | Leu  | Arg  | Asn   | Leu        |       |
|     |   |      |       |      | 1101 | 185        |             |      |      |         | 190        |       |      |      |       | 195        | **    |
| 1   |   | Arg  | Leu   | Arg  | Leu  | Ile        | Ser         | Arg  | Pro  | Thr     | Cys        | Asn   | Cys  | Ile  | Tyr   | Asn        |       |
|     | • |      |       | ,    |      | 200        |             |      |      |         | 205        |       |      | •    |       | 210        |       |
|     |   | Gln  | Leu   | His  | Gln  | Arg        | His         | Leu  | Ser  | Asn     |            |       | Arg  | Pro  | Gly   |            |       |
|     |   |      |       |      |      | 215        |             |      |      |         | 220        |       |      |      | •     | 225        |       |
|     |   | Leu  | Cys   | Gly  | Gly  |            | Gln         | Pro  | Gly  | Val     |            |       | Pro  | Cys  | Gln   | Gly        |       |
|     |   |      |       |      |      | 230        |             |      |      |         | 235        |       |      |      | •     | 240        | ov.   |
|     |   | Asp  | Ser   | Gly  | Gly  |            | Val         | Leu  | Cys  | Leu     | Glu<br>250 |       | Asp  | Gly  | His   | Trp<br>255 |       |
|     |   |      |       |      |      | 245        |             |      |      |         |            |       |      |      |       |            |       |
|     |   | Val  | Gln   | Ala  |      | 11e<br>260 | Ile         | Ser  | Phe  | Ala     | Ser<br>265 |       | Cys  | Ala  | Gln   | Glu<br>270 |       |
|     |   |      |       | _    |      |            |             |      | _    | <b></b> |            |       | n: - | 0    | 2     |            |       |
|     |   | Asp  | Ala   | Pro  | Val  | Leu<br>275 |             | Thr  | Asn  | Thr     | A1a<br>280 | Ala   | His  | Ser  | Ser   | Trp<br>285 |       |
|     |   | T 0  | C1 =  | 70 1 | Arg  | 17-1       | Cln         | C1,, | NΊο  | Λlà     | Dha        | T.A.i |      | Gln  | Ser   | Pro        |       |
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|     |   | Glu  | Thr   | Pro  | Glu  | Met        | Ser         | Asp  | Glu  | Asp     | Ser        | Cvs   | Val  | Àla  | Cvs   | Gly        |       |
|     |   | Jiu  | - 114 | -10  | JIU  | 305        |             |      | u    |         | 310        |       |      |      | - 1 - | 315        |       |
| •   |   |      |       |      |      |            |             | •    | ,    |         |            |       |      |      |       |            |       |
|     |   |      | •     |      |      |            |             |      |      |         |            |       |      |      |       |            |       |
|     |   |      |       |      |      |            |             |      | ,    |         |            |       |      |      |       |            |       |
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 Ala Thr Leu Cys Cys Ser Phe Ser Pro Glu Pro Gly Phe Ser Leu
 Ala Gln Leu Asn Leu Ile Trp Gln Leu Thr Asp Thr Lys Gln Leu
 Val His Ser Phe Ala Glu Gly Gln Asp Gln Gly Ser Ala Tyr Ala
 Asn Arg Thr Ala Leu Phe Pro Asp Leu Leu Ala Gln Gly Asn Ala
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 Pro Asn Lys Asp Leu Arg Pro Gly Asp Thr Val Thr Ile Thr Cys
 Ser Ser Tyr Gln Gly Tyr Pro Glu Ala Glu Val Phe Trp Gln Asp
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 Gly Gln Gly Val Pro Leu Thr Gly Asn Val Thr Thr Ser Gln Met
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220

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Val Leu Gln Lys Pro Phe Ile Cys His Arg Lys Thr Lys Gly Gly 35 40 45

Asp Leu Met Leu Val His Tyr Glu Gly Tyr Leu Glu Lys Asp Gly 50 5,5 60

Ser Leu Phe His Ser Thr His Lys His Asn Asn Gly Gln Pro Ile 65 70 75

Trp Phe Thr Leu Gly Ile Leu Glu Ala Leu Lys Gly Trp Asp Gln 80 85 90

Gly Leu Lys Gly Met Cys Val Gly Glu Lys Arg Lys Leu Ile Ile 95 . 100 105

Pro Pro Ala Leu Gly Tyr Gly Lys Glu Gly Lys Gly Lys Ile Pro 110 115 120

Pro Glu Ser Thr Leu Ile Phe Asn Ile Asp Leu Leu Glu Ile Arg 125 130 135

Asn Gly Pro Arg Ser His Glu Ser Phe Gln Glu Met Asp Leu Asn 140 145 150

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Ala Arg Leu Pro Cys Thr Phe Asn Ser Cys Tyr Thr Val Asn His 50 55 60

Lys Gln Phe Ser Leu Asn Trp Thr Tyr Gln Glu Cys Asn Asn Cys 65 70 75

Ser Glu Glu Met Phe Leu Gln Phe Arg Met Lys Ile Ile Asn Leu 80 85 90

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Ser Lys Tyr Asp Val Ser Val Met Leu Arg Asn Val Gln Pro Glu

<sup>&</sup>lt;210> 150

<sup>&</sup>lt;211> 215

<sup>&</sup>lt;212> PRT

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His Arg Gly His Gly Lys fle His Leu Gln Val Leu Met Glu Glu
140 145 150

Pro Pro Glu Arg Asp Ser Thr Val Ala Val Ile Val Gly Ala Ser 155 160 165

Val Gly Gly Phe Leu Ala Val Val Ile Leu Val Leu Met Val Val 170 175 180

Lys Cys Val Arg Arg Lys Lys Glu Gln Lys Leu Ser Thr Asp Asp 185 190 195

Leu Lys\_Thr Glu Glu Glu Gly Lys Thr Asp Gly-Glu Gly Asn Pro 200 205 210

Asp Asp Gly Ala Lys 215

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geeetgeett eageeteaeg gggeteagte tettttete tttggtgeea 200
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aaceacaaae agtteteeet gaaetggaet taeeaggagt geaaeaaetg 350
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<212> DNA

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|---------------------------|----------------|--------|-------|-------------|-----|-------|------|-------|------------|------|------|-----|-----|------------|
| <400><br>Met<br>1         |                |        | His   | Leu<br>5    | Arg | Pro   | Tyr  | Arg   | Val<br>10  | Gly  | Leu  | Leu | Pro | Asp<br>15  |
| Gly                       | Leu            | Leu    | Phe   | Leu<br>20   | Leu | Leu   | Leu  | Leu   | Met<br>25  | Leu  | Leu  | Ala | Asp | Pro<br>30  |
| Ala                       | Leu            | Pro    | Ala   | Gly<br>. 35 | Arg | His   | Pro  | Pro   | Val<br>40  |      | Leu  | Val | Pro | Gly<br>45  |
| _Asp                      | Leu            | Gly    | .Asn  | Gln<br>50   | Leu | -Glu- | Ala  | -Lys- | Leu<br>55  | -Asp | Lys  | Pro | Thr | Val<br>60  |
| .Val                      | His            | Tyr    | Leu   | Cys<br>65   | Ser | Lys   | Lys  | Thr   | Glu<br>70  | Ser  | Tyr  | Phe | Thr | Ile<br>75  |
| Trp                       | Leu            | Asn    | Leu   | Glu<br>80   | Leu | Leu   | Leu  | Pro   | Val<br>85  | Ile  | Ile  | Asp | Cys | Trp<br>90  |
| Ile                       | Asp            | Asn    | Ile   | Arg<br>95   | Leu | Val   | Tyr  | Asn   | Lys<br>100 | Thr  | Ser  | Arg | Ala | Thr<br>105 |
| Gln                       | Phe            | Pro    | Asp   | Gly<br>110  | Val | Asp   | Val  | Arg   | Val<br>115 | Pro  | ,Gly | Phe | Gly | Lys<br>120 |
| Thr                       | Phe            | Ser    | Leu   | Glu<br>125  | Phe | Leu   | Asp  | Pro   | Ser<br>130 | Lys  | Ser  | Ser | Val | Gly<br>135 |
| Ser                       | Tyr            | Phe    | His   | Thr<br>140  | Met | Val   | Glu  | Ser   | Leu<br>145 | Val  | Gly  | Trp | Gly | Tyr<br>150 |
| Thr                       | Årg            | Gly    | Glu   | Asp<br>155  | Val | Arg   | Gly  | Ala   | Pro<br>160 | Tyr  | Asp  | Trp | Arg | Arg<br>165 |
| Ala                       | Pro            | Asn    | Glu   | Asn<br>170  | Gly | Pro   | Tyr  | Phe   | Leu<br>175 | Ala  | Leu  | Arg | Glu | Met<br>180 |
| Ile                       | Glu            | Glu    | Met   | Tyr<br>185  | Gln | Leu   | Tyr  | Gly   | Gly<br>190 | Pro  | Val  | Val |     | Val<br>195 |
| Ala                       | His            | Ser    | Met   | Gly<br>200  | Asn | Met   | Tyr  | Thr   | Leu<br>205 | Tyr  | Phe  | Leu |     | Arg<br>210 |
| Gln                       | Pro            | Gln    | Ala   | Trp<br>215  | Lys | Asp   | Lys  | Tyr   | Ile<br>220 | Arg  | Ala  | Phe | Val | Ser<br>225 |
| Leu                       | Gly            | Ala    | Pro   | Trp<br>230  | Gly | Gly   | Val. | Ala   | Lys<br>235 | Thr  | Leu  | Arg | Val | Leu<br>240 |
| Ala                       | Ser            | Gly    | Asp   | Asn         | Asn | Arg   | Ile  | Pro   | Val        | Ile  | Gly  | Pro | Leu | Lys        |

|                              |              |      |       |             |        |        |     |          |             |     | ,   |      |      |              |     |
|------------------------------|--------------|------|-------|-------------|--------|--------|-----|----------|-------------|-----|-----|------|------|--------------|-----|
| Ile                          | Arg          | Glu  | Gln   | Gln<br>260  | Arg    | Ser    | Ala | Val      | Ser<br>265  | Thr | Ser | Trp  | Leu  | Leu<br>270   |     |
| Pro                          | Tyr          | Asn  | Tyr   | Thr<br>275  | -      | Ser    | Pro | Glu      | Lys<br>280  | Val | Phe | Val  | Gln  | Thr<br>285   |     |
| Pro                          | Thr          | Ile  | Asn   | Tyr<br>290  | Thr    | Leu    | Arg | Asp      | Tyr<br>295  | Arg | Lys | Phe  |      | Gln<br>300   |     |
| Asp                          | Ile          | Gly  | Phe   | Glu<br>305  | Asp    | Gly    | Trp | Leu      | Met<br>310  | Arg | Gln | Asp  | Thr  | Glu<br>315   |     |
| Gly                          | Leu          | Val  | Glu   | Ala<br>320  | Thr    | Met    | Pro | Pro      | Gly<br>325  |     | Gln | Leu  | His  | Cys<br>330   |     |
| .Leu.                        | Tyr          | Gly- | - Thr | -Gly<br>335 | -Va·l- | Pro    | Thr | Pro      | -Asp<br>340 | Ser | Phe | -Tyr | Tyr  | -Glu-<br>345 |     |
| Ser                          | Phe          | Pro  | Asp   | Arg<br>350  | Asp    | Pro    | Lys | Ile      | Cys<br>355  | Phe | Gly | Asp  | Gly  | Asp<br>360   |     |
| Gly                          | Thr          | Val  | Asn   | Leu<br>365  | Lys    | Ser    | Ala | Leu      | Gln<br>370  | Cys | Gln | Ala  | Trp  | Gln<br>375   |     |
| Ser                          | Arg          | Gln  | Glu   | His<br>380  | Gln    | Val    | Leu | Leu      | Gln<br>385  | Glu | Leu | Pro  | Gly  | Ser<br>390   |     |
| Glu                          | His          | Ile  | Glu   | Met<br>395  | Leu    | Ala    | Asn | Ala      | Thr<br>400  | Thr | Leu | Ala  | ·Tyr | Leu<br>405   |     |
| Lys                          | Arg          | Val  | Leu   | Leu<br>410  | Gly    | Pro    |     | ·        |             |     | •   |      |      |              |     |
| <210<br><211<br><212<br><213 | > 23<br>> DN | A.   | cial  | Seq         | uenc   | e      |     |          |             |     |     |      |      |              |     |
| <22 <u>.</u> 0<br><223       |              | nthe | tic   | olig        | onuc   | leot   | ide | prob     | e ·         | ·   |     |      |      |              |     |
| <400<br>ctg                  |              |      | acac  | gggg        | tg a   | gg 2   | 3   | <i>:</i> |             | •   |     |      | . ,  | ,            | . • |
| <210<br><211<br><212<br><213 | > 24<br>> DN | A    | cial  | Seq         | uenc   | e<br>e |     |          |             |     |     |      |      | ,            |     |
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<210> 162

<211> 224

<212> PRT

<213> Homo sapiens ·

<400> 162

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Asp Leu Arg Arg Phe Leu Thr Gln Pro Gln Val Val Ala Arg Ala 20 25 30

Val Cys Leu Val Phe Ala Leu Ile Val Phe Ser Cys Ile Tyr Gly
35 40 45

Glu Gly Tyr Ser Asn Ala His Glu Ser Lys Gln Met Tyr Cys Val 50 55 60

Phe Asn Arg Asn Glu Asp Ala Cys Arg Tyr Gly Ser Ala Ile Gly
65 70 75

Val Leu Ala Phe Leu Ala Ser Ala Phe Phe Leu Val Val Asp Ala 80 85 90

Tyr Phe Pro Gln Ile Ser Asn Ala Thr Asp Arg Lys Tyr Leu Val 95 100 105

Ile Gly Asp Leu Leu Phe Ser Ala Leu Trp Thr Phe Leu Trp Phe 110 115 120

Val Gly Phe Cys Phe Leu Thr Asn Gln Trp Ala Val Thr Asn Pro 125 130 135

Lys Asp Val Leu Val Gly Ala Asp Ser Val Arg Ala Ala Ile Thr 140 145 150

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Phe Ser Phe Phe Ser Ile Phe Ser Trp Gly Val Leu Ala Ser Leu
Ala Tyr Gln Arg Tyr Lys Ala Gly Val Asp Asp Phe Ile Gln Asn
Tyr Val Asp Pro Thr Pro Asp Pro Asn Thr Ala Tyr Ala Ser Tyr
Pro Gly Ala Ser Val Asp Asn Tyr Gln Gln Pro Pro Phe Thr Gln
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Asn Ala Glu Thr Thr Glu Gly Tyr Gln Pro Pro Pro Val Tyr
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<210> 167
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<220>
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<400> 168

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<210> 169

<211> 802

<212> PRT

<213> Homo sapiens

<400> 169

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Gly Gly Asp Gly Glu Glu Ala Glu Pro Glu Gly Met Phe Lys Ala 20 25 30

Cys Glu Asp Ser Lys Arg Lys Ala Arg Gly Tyr Leu Arg Leu Val
35 40 45

Pro Leu Phe Val Leu Leu Ala Leu Leu Val Leu Ala Ser Ala Gly
50 55 60

Val Leu Leu Trp Tyr Phe Leu Gly Tyr Lys Ala Glu Val Met Val
65 70 75

Ser Gln Val Tyr Ser Gly Ser Leu Arg Val Leu Asn Arg His Phe 80 85 90

Ser Gln Asp Leu Thr Arg Arg Glu Ser Ser Ala Phe Arg Ser Glu

|     |     | •   |     |            |      |      |     |     |            |     |      |     |       |             |
|-----|-----|-----|-----|------------|------|------|-----|-----|------------|-----|------|-----|-------|-------------|
| Thr | Ala | Lys | Aŀa | Gln<br>110 | Lys  | Met  | Leu | Lys | Glu<br>115 | Leu | Ile  | Thr | Şer   | Thr<br>120  |
| Arg | Leu | Gly | Thr | Tyr<br>125 | Tyr  | Asn  | Ser | Ser | Ser<br>130 | Val | Tyr  | Ser | Phe   | Gly<br>135  |
| Ģlu | Gly | Pro | Leu | Thr<br>140 | Cys  | Phe  | Phe | Trp | Phe<br>145 | Ile | Leu  | Gln | Ile   | Pro<br>150  |
| Glu | His | Arg | Arg | Leu<br>155 | Met  | Leu  | Ser | Pro | Glu<br>160 | Val | Val  | Gln | Ala   | Leu<br>165  |
| Leu | Val | Glu | Glu | Leu<br>170 | Leu  | Ser  | Thr | Val | Asn<br>175 | Ser | Ser  | Ala | Ala   | Val<br>180  |
| Pro | Tyr | Arg | Ala | Glu<br>185 | Tyr. | Glu  | Уаļ | Ąsp | Pro<br>190 | Glu | Gly. | Leu | _Val- | Ile-<br>195 |
| Leu | Glu | Ala | Ser | Val<br>200 | Lys  | Asp  | Ile | Ala | Ala<br>205 | Leu | Asn  | Ser | Thr   | Leu<br>210  |
| Gly | Cys | Tyr | Arg | Tyr<br>215 | Ser  | Tyr  | Val | Gly | Gln<br>220 | Gly | Gln  | Val | Leu   | Arg<br>225  |
| Leu | Lys | Gly | Pro | Asp<br>230 | His  | Leu  | Ala | Ser | Ser<br>235 | Cys | Leu  | Trp | His   | Leu<br>240  |
| Gln | Gly | Pro | Lys | Asp<br>245 | Leu  | Met  | Leu | Lys | Leu<br>250 | Arg | Leu  | Glu | Trp   | Thr<br>255  |
| Leu | Ala | Glu | Cys | Arg<br>260 | Asp  | ·Arg | Leu | Ala | Met<br>265 | Tyr | Asp  | Val | Ala   | Gly<br>270  |
| Pro | Leu | Glu | Lys | Arg<br>275 | Leu  | Ile  | Thr | Ser | Val<br>280 | Tyr | Gly  | Cys | Ser   | Arg<br>285  |
| Gln | Glu | Pro | Val | Val<br>290 | Glu  | Val  | Leu | Ala | Ser<br>295 | Gly | Ala  | Ile | Met   | Ala<br>300  |
| Val | Val | Trp | Lys | Lys<br>305 | Gly  | Leu  | His | Ser | Tyr<br>310 | Tyr | Asp  | Pro | Phe   | Val<br>315  |
| Leu | Ser | Val | Gln | Pro<br>320 | Val  | Val  | Phe | Gln | Ala<br>325 | Cys | Glu  | Val | Asn   | Leu<br>330  |
| Thr | Lęu | Asp | Asn | Arg<br>335 | Leu  | Asp  | Ser | Gln | Gly<br>340 | Val | Leu  | Ser | Thr   | Pro<br>345  |
| Tyr | Phe | Pro | Ser | Tyr<br>350 | Tyr  | Ser  | Pro | Gln | Thr<br>355 | His | Cys  | Ser | Trp   | His<br>360  |
| Leu | Thr | Val | Pro | Ser<br>365 | Leu  | Asp  | Tyr | Gly | Leu<br>370 | Ala | Leu  | Trp | Phe   | Asp<br>375  |
| Ala | Tyr | Ala | Leu | Arg        | Arg  | Gln  | Lys | Tyr | Asp        | Leu | Pro  | Cys | Thr   | Gln         |
|     |     |     |     |            |      |      |     |     |            |     |      |     |       |             |

Arg Pro Val Cys Leu Pro Ala Arg Ser His Phe Phe Glu Pro Gly 680 685 690

Leu His Cys Trp Ile Thr Gly Trp Gly Ala Leu Arg Glu Gly Gly 695 700 705

Pro Ile Ser Asn Ala Leu Gln Lys Val Asp Val Gln Leu Ile Pro 710 715 720

Gln Asp Leu Cys Ser Glu Ala Tyr Arg Tyr Gln Val Thr Pro Arg 725 730 735

Met Leu Cys Ala Gly Tyr Arg Lys Gly Lys Lys Asp Ala Cys Gln 740 745. 750

Gly Asp Ser Gly Gly Pro Leu Val Cys Lys Ala Leu Ser Gly Arg 755 760 765

Trp Phe Leu Ala Gly Leu Val Ser Trp Gly Leu Gly Cys Gly Arg
770 775 780

Pro Asn Tyr Phe Gly Val Tyr Thr Arg Ile Thr Gly Val Ile Ser 785 790 795

Trp Ile Gln Gln Val Val Thr

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<211> 1327-

<212> DNA

<213> Homo sapiens

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tgeactatgg cttgtacaac cagteggaee eetgeeetgg agagtteete 200
tgttetgta atggaetetg tgteeetgee tgtgatgggg teaaggaetg 250
ceecaaegge etggatgaga gaaaetgegt ttgeagagee acatteeagt 300
geaaagagga cageacatge ateteaetge eeaaggtetg tgatgggeag 350
cetgattgte teaaeggeag egatgaagag eagtgeeagg aaggggtgee 400
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gageactgtg aetgtggeet eeaaggeeee teeageega ttgttggtgg 550

agetgtgtee teegagggtg agtggeeatg geaggeeage eteeaggtte 600 ggggtcgaca catctgtggg ggggccctca tcgctgaccg ctgggtgata 650 acagetgeec actgetteea ggaggaeage atggeeteea eggtgetgtg 700 gaccgtgttc ctgggcaagg tgtggcagaa ctcgcgctgg cctggagagg 750 tgtccttcaa ggtgagccgc ctgctcctgc acccgtacca cgaagaggac 800 agccatgact acgacgtggc gctgctgcag ctcgaccacc cggtggtgcg 850 ctcggccgcc gtgcgccccg tctgcctgcc cgcgcgctcc cacttcttcg 900 ageceggeet geactgetgg attacggget ggggegeett gegegaggge 950 ggccccatca gcaacgctct gcagaaagtg gatgtgcagt tgatcccaca 1000 ggacctgtgc agcgaggcct atcgctacca ggtgacgcca cgcatgctgt 1050 gtgccggcta ccgcaagggc aagaaggatg cctgtcaggg tgactcaggt 1100 ggtccgctgg tgtgcaaggc actcagtggc cgctggttcc tggcggggct 1150 ggtcagctgg ggcctgggct gtggccggcc taactacttc ggcgtctaca 1200 cccgcatcac aggtgtgatc agctggatcc agcaagtggt gacctgagga 1250 actgccccc tgcaaagcag ggcccacctc ctggactcag agagcccagg 1300 gcaactgcca agcaggggga caagtat 1327 <210> 171 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 171 taacagctgc ccactgcttc cagg 24 <210> 172 <211> 22 <212> DNA <213> Artificial Sequence

<220>

<400> 172

<210> 173 <211> 50 <212> DNA

<223> Synthetic oligonucleotide probe

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<223> Synthetic oligonucleotide probe
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<210> 174
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- tgcctatgca ctgaggaggc agaag 25 -
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<210> 176
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 ctccagtccc ccagccctg gccgagagaa gggtcttacc ggccgggatt 150
 gctggaaaca ccaagaggtg gtttttgttt tttaaaactt ctgtttcttg 200
 ggaggggtg tggcggggca ggatgagcaa ctccgttcct ctgctctgtt 250
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<sup>&</sup>lt;210> 178

<sup>&</sup>lt;211> 354

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|   | <400><br>Met |         |     | Ser | Val        | Pro | Leu | Leu | Cys | Phe               | Trp | Ser      | Leu | Cys |                 |     |     |     |    |     |
|---|--------------|---------|-----|-----|------------|-----|-----|-----|-----|-------------------|-----|----------|-----|-----|-----------------|-----|-----|-----|----|-----|
|   | l<br>Cys     | Phe     | Ala | Ala | Gly<br>20  | Ser | Pro | Val | Pro | 10<br>Phe<br>25   | Gly | Pro      | Glu | Gly | 15<br>Arg<br>30 |     |     |     |    |     |
|   | Leu          | .Glu    | Asp | Lys | Leu<br>35  | His | Lys | Pro | Lys | Ala<br>40         | Thṛ | Gln      | Thr | Glu | Val<br>45       |     |     |     |    |     |
|   | Lys          | Pro     | Ser | Val | Arg<br>50  | Phe | Asn | Leu | Arg | Thr<br>55         | Ser | Lys      | Asp | Pro | Glu<br>60       |     | · . |     |    |     |
|   |              |         |     |     | 65         |     |     |     |     | His<br>70         |     |          |     | ٠   | .75             |     |     |     |    |     |
| - · · · · · · · · · · · · · · · · · · · | Asp          | Cys<br> | Ser |     |            |     |     |     |     | Thr<br>-85        |     |          |     |     | His<br>-90      |     |     |     |    | · · |
| •                                       | Gly          | Trp     | Thr | Met | Ser<br>95  | Gly | Ile | Phe | Glu | Asn<br>100        | Trp | Leu      | His | Lys | Leu<br>105      |     |     |     | o. |     |
|   |              |         |     |     | 110        |     |     |     | ,   | Asp<br>115        |     |          | :   | 4   | 120             |     |     |     |    |     |
|   |              | ÷       |     |     | 125        |     |     |     |     | Leu<br>130        | ,   |          |     |     | 135             |     |     |     |    |     |
|   |              |         |     |     | 140        |     |     |     |     | Ile<br>145        |     |          |     |     | 150             |     |     |     |    |     |
|   | ı            |         |     | 4   | 155        | 1,  |     |     |     | Leu<br>160<br>Ala |     |          |     |     | 165             |     |     | • . |    |     |
| • •                                     |              | ٠,      |     |     | 170        |     |     | ,   |     | 175               |     | . 1      |     |     | 180             |     |     |     |    |     |
| *                                       | Phe          | Val     | Lys | Gly | Thr<br>185 | Val | Gly | Arg | Ile | Thr<br>190        | Gly | Leu      | Asp | Pro | Ala<br>195      |     |     |     |    |     |
|   | Gly          | Pro     | Met | Phe | Glu<br>200 | Gly | Ala | Asp | Ile | His<br>205        | Lys | Arg      | Leu |     | Pro<br>210      | : * | ·   |     |    |     |
| * .                                     | Asp          | Asp     | Ala | Asp | Phe<br>215 | Val | Asp | Val | Leu | His<br>220        | Thr | Tyr      | Thr | Arg | Ser<br>225      |     |     |     |    |     |
|   | Phe          | Gly     | Leu | Ser | Ile<br>230 | Gly | Ile | Gln | Met | Pro<br>235        | Val | Gľy      | His | Ile | Asp<br>240      |     |     |     |    |     |
|   | Ile          | Tyr     | Pro | Asn | Gly<br>245 | Gly | Asp | Phe | Gln | Pro<br>250        | Gly | Cys<br>: | Gly | Leu | Asn<br>255      |     |     |     |    |     |
|   | Asp          | Val     | Leu | Gly | Ser<br>260 | Ile | Ala | Tyr | Gly | Thr<br>265        |     | Thr      | Glù | Val | Val<br>270      | •   |     |     |    |     |
|   | Lys          | Cys     | Glu | His | Glu<br>275 | Arg | Ala | Val | His | Leu<br>280        | Phe | Val      | Asp | Ser | Leu<br>285      |     |     |     |    |     |

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Cys Asn Ser Ile Gly Tyr Asn Ala Lys Lys Met Arg Asn Lys Arg
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Leu Val Arg Asp Ser Arg Thr Ser Pro Ala Asn Cys Thr Trp Leu
50 55 60

Ile Leu Gly Ser Lys Glu Gln Thr Val Thr Ile Arg Phe Gln Lys
65 70 75

Leu His Leu Ala Cys Gly Ser Glu Arg Leu Thr Leu Arg Ser Pro 80 85 90

Leu Gln Pro Leu Ile Ser Leu Cys Glu Ala Pro Pro Ser Pro Leu
95 100 105

Gln Leu Pro Gly Gly Asn Val Thr Ile Thr Tyr Ser Tyr Ala Gly
110 115 120

Ala Arg Ala Pro Met Gly Gln Gly Phe Leu Leu Ser Tyr Ser Gln 125 130 135

Asp Trp Leu Met Cys Leu Gln Glu Glu Phe Gln Cys Leu Asn His 140 145 150

Arg Cys Val Ser Ala Val Gln Arg Cys Asp Gly Val Asp Ala Cys 155 160 165

Gly Asp Gly Ser Asp Glu Ala Gly Cys Ser Ser Asp Pro Phe Pro 170 175 180

Gly Leu Thr Pro Arg Pro Val Pro Ser Leu Pro Cys Asn Val Thr

200 205 210

Leu Ala Ser Val Ser His Pro Gln Ser Cys His Trp Leu Leu Asp 215 220 225

Pro His Asp Gly Arg Arg Leu Ala Val Arg Phe Thr Ala Leu Asp 230 235 240

Leu Gly Phe Gly Asp Ala Val His Val Tyr Asp Gly Pro Gly Pro 245 250 255

Pro Glu Ser Ser Arg Leu Leu Arg Ser Leu Thr His Phe Ser Asn 260 265 270

Gly Lys\_Ala\_Val\_Thr Val Glu Thr Leu Ser Gly Gln Ala Val Val 275 280 285

Ser Tyr His Thr Val Ala Trp Ser Asn Gly Arg Gly Phe Asn Ala 290 295 300

Thr Tyr His Val Arg Gly Tyr Cys Leu Pro Trp Asp Arg Pro Cys 305 310

Gly Leu Gly Ser Gly Leu Gly Ala Gly Glu Gly Leu Gly Glu Arg 320 325 330

Cys Tyr Ser Glu Ala Gln Arg Cys Asp Gly Ser Trp Asp Cys Ala 335 340 345

Asp Gly Thr Asp Glu Glu Asp Cys Pro Gly Cys Pro Pro Gly His 350 355 360

Phe Pro Cys Gly Ala Ala Gly Thr Ser Gly Ala Thr Ala Cys Tyr 365 370 375

Leu Pro Ala Asp Arg Cys Asn Tyr Gln Thr Phe Cys Ala Asp Gly 380 385 390

Ala Asp Glu Arg Arg Cys Arg His Cys Gln Pro Gly Asn Phe Arg 395 400 405

Cys Arg Asp Glu Lys Cys Val Tyr Glu Thr Trp Val Cys Asp Gly 410 415

Gln Pro Asp Cys Ala Asp Gly Ser Asp Glu Trp Asp Cys Ser Tyr 425 430 430

Val Leu Pro Arg Lys Val Ile Thr Ala Ala Val Ile Gly Ser Leu

Val Cys Gly Leu Leu Leu Val Ile Ala Leu Gly Cys Thr Cys Lys 455 460 465

Leu Tyr Ala Ile Arg Thr Gln Glu Tyr Ser Ile Phe Ala Pro Leu

| Ser          | Arg   | Met   | Glu  | 485        | GIu  | lle     | Val    | Gln  | Gln<br>490  | Gln | Ala | Pro   | Pro | Ser<br>495 |
|--------------|-------|-------|------|------------|------|---------|--------|------|-------------|-----|-----|-------|-----|------------|
| Tyr          | Gly   | Gln   | Leu  | Ile<br>500 | Ala  | Gln     | Gly    | Ala  | Ile<br>505  | Pro | Pro | Val   | Glu | Asp<br>510 |
| Phe          | Pro   | Thr   | Glu  | Asn<br>515 | Pro  | Asn     | Asp    | Asn  | Ser<br>520  | Val | Leu | Gly   | Asn | Leu<br>525 |
| Arg          | Ser   | Leu   | Leu  | Gln<br>530 | Ile  | Leu     | Arg    | Gln  | Asp<br>535  | Met | Thr | Pro   | Gly | Gly<br>540 |
| Gly          | Pro   | Gly   | Ala  | Arg<br>545 | Arg  | Arg     | Gln    | Arg  | Gly<br>550  |     | Leu | Met   | Arg | Arg<br>555 |
| Leu          | _Val_ | Arg   | _Arg | Leu<br>560 | Arg. | Arg     | Trp    | Gly  | Leu-<br>565 | Leu | Pro | -Arg  | Thr | Asn<br>570 |
| Thr          | Pro   | Ala   | Arg  | Ala<br>575 | Ser  | Ģlu     | Ala    |      | Ser<br>580  | Gln | Val | Thr   | Pro | Ser<br>585 |
| Ala          | Ala   | Pro   | Leu  | Glu<br>590 | Ala  | Leu     | Asp    | Gly  | Gly<br>595  | Thr | Gly | Pro   | Ala | Arg<br>600 |
| Glu          | Gly   | Gly   | Ala  | Val<br>605 | Gly  | Gly     | Gln    | Asp  | Gly<br>610  | Glu | Gln | Ala   | Pro | Pro<br>615 |
| Leu          | Pro   | Ile   | Lys  | Ala<br>620 | Pro  | Leu     | Pro    | Ser  | Ala<br>625  | Ser | Thr | Ser   | Pro | Ala<br>630 |
| Pro          | Thr   | Thr   | Val  | Pro<br>635 | Glu  | Ala     | Pro    | Gly  | Pro<br>640  | Leu | Pro | Ser   | Leu | Pro<br>645 |
| Leu          | Glu   | Pro   | Ser  | Leu<br>650 | Leu  | Ser     | Gly    | Val  | Val<br>655  | Gln | Ala | Leu   | Arg | Gly<br>660 |
| Arg          | Leu   | Leu   | Pro  | Ser<br>665 | Leu  | Gly     | Pro    | Pro  | Gly<br>670  | Pro | Thr | Arg   | Ser | Pro<br>675 |
| Pro          | Gly   | Pro   | His  | Thr<br>680 | Ala  | Val     | Leu    | Ala  | Leu<br>685  | Glu | Asp | Glu   | Asp | Asp<br>690 |
| Val          | Leu   | Leu   | Val  | Pro<br>695 | Leu  | Ala     | Glu    | Pro  | Gly<br>700  | Val | Trp | Val   | Ala | Glu<br>705 |
| Ala          | Glu   | Asp   | Glu  | Pro<br>710 | Leu  | Leu     | Thr    |      |             |     |     | • . • |     |            |
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| <212<br><213 |       |       | cial | Séa        | uenc | e .     |        | •    |             |     |     |       |     |            |
|              |       |       |      |            |      | -       |        |      |             |     |     |       |     | ,          |
| <220         |       | -4-L- |      | _1/.       |      | د د م 1 | - نہ ا | - L  | ,           |     |     |       |     |            |
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Thr Ser Met Thr Phe Phe Ile Ile Ala Gln Ala Pro Glu Pro Tyr 35 40 45

Ile Val Ile Thr Gly Phe Glu Val Thr Val Ile Leu Phe Phe Ile
50 55 60

Leu Leu Tyr Val Leu Arg Leu Asp Arg Leu Met Lys Trp Leu Phe . . . 65 70 75

Trp Pro Leu Leu Asp Ile Ile Asn Ser Leu Val Thr Thr Val Phe
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Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu Thr Thr Thr 95 100 105

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<211> 518

<212> PRT.

<213> Homo sapien

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20 25 30

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Thr Pro Gly Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu
50 55 60

| Ala | Leu | Ala | Leu | Glu<br>65  | Pro | Ala | Leu | Ala | Ser<br>70   | Pro | Ala  | Gly | Ala              | Ala<br>75  |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|-------------|-----|------|-----|------------------|------------|
| Asn | Phe | Leu | Ala | Met<br>80  | Val | Asp | Asn | Leu | Gln<br>85   | Gly | Asp  | Ser | Gly              | Arg<br>90  |
| Gly | Tyr | Tyr | Leu | Glu<br>95  | Met | Leu | Ile | Gly | Thr         | Pro | Pro  | Gln | Lys              | Leu<br>105 |
| Gln | Ile | Leu | Val | Asp<br>110 | Thr | Gly | Ser | Ser | Asn<br>115  | Phe | Ala  | Val | Ala              | Gly<br>120 |
| Thr | Pro | His | Ser | Tyr<br>125 | Ile | Asp | Thr | Tyr | Phe<br>130  | Asp | Thr  | Glu | Arg <sub>.</sub> | Ser<br>135 |
| Ser | Thr | Tyr | Arg | Ser<br>140 | Lys | Gly | Phe | Asp | Val.<br>145 | Thr | Val  | Lys | Tyr              | Thr<br>150 |
| Gln | ĞÎy | Ser | _   | Thr<br>155 | Gly | Phe | Val | Gly | Glu<br>160  | Asp | Leu  | Val | Thr              | Ile<br>165 |
| Pro | Lys | Gly | Phe | Asn<br>170 | Thr | Ser | Phe | Leu | Val<br>175  | Asn | Ile  | Ala | Thr              | Ile<br>180 |
| Phe | Glu | Ser | Glu | Asn<br>185 | Phe | Phe | Leu | Pro | Gly<br>190  | Ile | .Lys | Trp | Asn              | Gly<br>195 |
| Ile | Leu | Gly | Leu | Ala<br>200 | Tyr | Ala | Thr | Leu | Ala<br>.205 | Lys | Pro  | Ser | Ser              | Ser<br>210 |
| Leu | Glu | Thr | Phe | Phe<br>215 | Asp | Ser | Leu | Val | Thr<br>220  | Gln | 'Ala | Asn | Ile              | Pro<br>225 |
| Asn | Val | Phe | Ser | Met<br>230 | Gln | Met | Cys | Gly | Ala<br>235  | Gly | Leu  | Pro | Val              | Ala<br>240 |
| Gly | Ser | Gly | Thr | Asn<br>245 | Gly | Gly | Ser | Leu | Val<br>250  | Leu | Gly  | Gly | Ile              | Glu<br>255 |
| Pro | Ser | Leu | Tyr | Lys<br>260 | Gly | Asp | Ile | Trp | Tyr<br>265  | Thr | Pro  | Ile | Lys<br>·         | Glu<br>270 |
| Glu | Trp | Tyr | Tyr | Gln<br>275 | Ile | Glu | Ile | Leu | Lys<br>280  | Leu | Glu  | Ile | Gly              | Gly<br>285 |
| Gln | Ser | Leu | Asn | Leu<br>290 | Asp | Cys | Arg | Glu | Tyr<br>295  | Asn | Ala  | Asp | Lys              | Ala<br>300 |
| Ile | Val | Asp | Ser | Gly<br>305 | Thr | Thr | Leu | Leu | Arg<br>310  | Leu | Pro  | Gln | Lys              | Val<br>315 |
| Phe | Asp | Ala | Val | Val<br>320 | Glu | Ala | Val | Ala | Arg<br>325  |     | Ser  | Leu | Ile              | Pro<br>330 |
| Glu | Phe | Ser | Asp | Gly<br>335 | Phe | Trp | Thr | Gly | Ser<br>340  | Gln | Leu  | Ala | Cys              | Trp<br>345 |
|     |     |     |     |            |     |     |     |     |             |     |      |     |                  |            |

11 1.

|                                       |                |              |        |       |              |        |                |        |         |       |          | •        | ٠       |       |            |       |     |
|---------------------------------------|----------------|--------------|--------|-------|--------------|--------|----------------|--------|---------|-------|----------|----------|---------|-------|------------|-------|-----|
|                                       | •              |              |        |       |              |        |                |        |         |       |          |          |         |       |            |       |     |
|                                       |                |              |        |       |              |        | •              |        |         |       |          |          |         |       |            |       |     |
|                                       | Thr            | Asn          | Ser    | Glu   | Thr          | Pro    | Trp            | Ser    | Tvr     | Phe   | Pro      | Lvs      | Tle     | Ser   | Ile        | •     |     |
|                                       |                |              |        |       | 350          |        | •              |        | 2       | 355   |          | 2,0      | +10     | . Der | 360        |       |     |
|                                       | Tyr            | Leu          | Āra    | Asp   | Glu          | Żen    | Sar            | °      | 7       |       | D1       |          |         | 0     |            |       |     |
| •                                     |                |              | • 9    | Asp   | 365          | non    | Ser            | ser    | Arg     | 370   | Phe      | Arg      | Ile     | Thr   |            |       |     |
|                                       | Ton            | D            | 01-    |       | _            |        |                |        |         |       | •        |          | -       |       | 375        |       |     |
|                                       | ьец            | P10          | GIN    | Leu   | Tyr<br>380   | Ile    | Gln            | Pro    | Met     | Met   | Gly      | Ala      | Gly     | Leu   |            |       |     |
| + 3.                                  |                |              |        |       |              |        |                |        |         | 385   |          |          |         |       | 390        | ٠.    |     |
|                                       | Tyr            | Glu          | Cys    | Tyr   | Arg          | Phe    | Gly            | Ile    | Ser     | Pro   | Ser      | Thr      | Asn     | Ala   | Leu        |       | •   |
|                                       |                |              |        |       | 395          |        |                |        |         | 400   |          |          |         |       | 405        |       |     |
|                                       | Val            | Ile          | Gly    | Ala   | Thr          | Val    | Met            | Glu    | Gly     | Phe   | Tvr      | Val      | Ile     | Phe   | Asn        |       | :   |
|                                       |                |              |        | · ·   | 410          |        |                | •      |         | 415   | <b>-</b> |          | ,       |       | 420        | •     |     |
|                                       | Arg            | Ala          | Gln    | Lys   | Ara          | Val    | Glv            | Phe    | ΔΙα     | λ1-   | ٠ ، .    | <br>Dana | <u></u> | ·     | ٠          |       |     |
|                                       |                | •            |        | -     | 425          | :      |                |        | nia     | 430   | Ser      | PIO      | Cys     | Ala   | G1u<br>435 | • 1.  |     |
|                                       | TIE            | <br>د ۱۵     | ัดเจ้า | 71.   | 71.          | 77-1   | - <u>-</u>     |        | .=      |       | <u></u>  |          |         |       |            |       | ·   |
|                                       |                |              | OTY    | VIG.  | 440          | vai    | ser            | GTÜ    | lle     | Ser.  | Gly      | Pro      | Phe     | Ser   | Thr        |       |     |
|                                       | άı             | _            |        |       |              |        |                |        |         |       |          |          |         |       | 450        |       | . 1 |
|                                       | GIU            | Asp          | Val    | Ala.  | Ser<br>455   | Asn    | Cys            | Val    | Pro     | Ala   | Gln      | Ser      | Leu     | Ser   | Glu        |       | ·   |
|                                       |                |              |        |       | ٠            |        |                |        |         | 460   |          |          |         |       | 465        | :     | • . |
|                                       | Pro            | Ile          | Leu    | Trp   | Ile          | Val    | Ser            | Tyr    | Ala     | Leu   | Met      | Ser      | Val     | Cys   | Glv        | ٠,    |     |
|                                       |                | :            | .'     | , ,   | 470          |        | 1              |        |         | 475   | :        |          | 181     |       | 480        |       |     |
|                                       | Ala            | Ile :        | Leu    | Leu   | Val          | Leu    | Ile            | Val    | Leu     | Leu   | Leu      | Len      | Pro     | Pho.  | Λ~~        | 0, 1  |     |
|                                       | ٠.             | ,<br>,       | - 5    | 4_    | 485          | ·. •   |                |        |         | 490   |          |          |         | 1116  | 495        |       |     |
| * .                                   | Cys            | Gln <i>i</i> | Arg    | Ard   | Pro          | Ara    | Asn            | Pró    | Glu     | W - 1 | Vo.1     | N        |         | ~     |            |       |     |
|                                       | -              | ٠            |        | : :   | 500          | · 9    | sp             | 110.   | GIU     | 505   | vaı      | Asn      | Asp     |       | Ser<br>510 |       |     |
|                                       | Ser I          |              | 7-1    | 71    | 14 -         | Ž      | _              | _      |         |       |          |          |         | ٠.    | 310        |       |     |
|                                       | Ser I          | ocu .        |        |       | 115 .<br>515 | Arg    | Trp            | Lys    |         |       | •        |          |         |       |            | χ     |     |
|                                       | 4010-          |              |        | •     |              |        |                |        |         |       |          |          |         | *     |            |       |     |
|                                       | <210>.         |              |        |       |              |        |                |        | :-      |       |          | · . ·    | 2. 1    |       |            | . ?   |     |
| * * * *                               | <212>          | DNA          |        |       |              |        |                | . +    |         |       |          | •        |         |       |            |       |     |
|                                       | <213>          | Arti         | fic    | ial S | Seque        | ence   |                |        | •       |       |          |          |         |       |            | ×     |     |
|                                       | (220>          | •            | : •    |       | • •          |        |                | .;     |         |       |          |          |         | , ,   |            |       | : : |
|                                       | (223>          | Synt         | heti   | ic ol | igor         | nucle  | eotic          | de pi  | robe    |       | Ē, '.    |          |         |       |            | · , . |     |
|                                       | (400>          |              |        |       |              |        |                | ,      |         |       |          |          |         |       |            |       | . , |
|                                       | cgcag          |              | tac    | agāt  | tete         | . a 2  | . 21           |        | *       |       | ٠, `     | 9        |         |       |            |       |     |
|                                       |                |              |        |       |              | . 7 4  | · <del>-</del> | . ,    |         | •     |          |          |         |       |            |       |     |
| · · · · · · · · · · · · · · · · · · · | 210><br>211>   | 198          |        |       |              |        | ٠.             |        | ٠.      |       | : :      |          |         |       |            |       |     |
|                                       | 212>           |              |        | :     |              |        |                | •      | e       |       |          |          |         |       |            |       |     |
|                                       | 213>           |              | fici   | al S  | eque         | nce    |                |        |         |       | , ÷.     |          |         |       |            |       |     |
| ,                                     | 220>           | •            | ,      |       |              |        |                |        |         |       |          |          |         |       | . "        | •     |     |
|                                       | 223>           | Syntl        | heti   | c ol  | iaon         | ucle   | otid           | le inn | ohe     |       |          |          |         |       | *          |       |     |
|                                       |                | ŕ            |        |       | ,            |        |                | PI     | ا میں د |       |          |          |         |       |            | - •   |     |
|                                       | 400><br>ggaaai |              | a ~~   |       |              | 10     | . :            |        |         |       |          |          |         |       |            |       | (   |
| ·                                     | - yuaa i       | - cyy        | . yg   | ccda  | ayc          | <br>TA | •              | • ;    |         |       | ٠.       |          | ·       |       |            |       |     |
|                                       |                |              |        |       |              |        |                |        |         |       |          |          | ٠.      | •     |            |       |     |
|                                       | ÷              |              |        | . •   |              |        |                |        |         |       |          |          |         |       |            |       |     |
|                                       |                |              |        |       |              | •      |                |        |         |       |          |          |         |       |            |       |     |
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<210> 202
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35 40 45

Ser Gly Ile Gly Lys Met Thr Ala Leu Glu Leu Ala Arg Arg Gly
50 55 60

Ala Arg Val Val Leu Ala Cys Arg Ser Gln Glu Arg Gly Glu Ala

|      |      |     |     |     |            |     |     |     |     |            |     |     |     | •   |            |   |   |     |      |   |   |   |
|------|------|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|---|---|-----|------|---|---|---|
|      |      |     |     |     |            |     |     |     |     |            |     |     |     |     |            |   |   |     |      | • |   |   |
|      | Ala  | Ala | Phe | Asp | Leu<br>80  | Arg | Gln | Glu | Ser | Gly<br>85  | Asn | Asn | Glu | Val | Ile<br>90  |   |   |     |      |   |   |   |
|      | Phe  | Met | Ala | Leu | Asp<br>95  | Leu | Ala | Ser | Leu | Ala<br>100 | Ser | Val | Arg | Ala | Phe<br>105 |   |   |     |      |   |   |   |
|      | Ala  | Thr | Ala | Phe | Leu<br>110 | Ser | Ser | Glu | Pro | Arg<br>115 | Leu | Asp | Ile | Leu | Ile<br>120 |   |   |     |      |   |   |   |
|      | His  | Asn | Ala | Gly | Ile<br>125 | Ser | Ser | Cys | Gly | Arg<br>130 | Thr | Arg | Glu | Ala | Phe<br>135 |   |   | ,   |      |   | , |   |
| - 8- | Asn  | Leu | Leu | Leu | Arg<br>140 | Val | Asn | His | Ile | Gly<br>145 | Pro | Phe | Leu | Leu | Thr<br>150 |   |   |     |      |   |   |   |
|      | His  | Leu | Leu | Leu | Pro<br>155 | Cys | Leu | Lys | Ala | Cys<br>160 | Ala | Pro | Ser | Arg | Val<br>165 |   | - | ) - | <br> | - |   |   |
|      | Val  | Val | Val | Ala | Ser<br>170 | Ala | Ala | His | Суѕ | Arg        | Gly | Arg | Leu | Asp | Phe<br>180 |   |   |     |      |   |   |   |
|      | Lys  | Arg | Leu | Asp | Arg<br>185 | Pro | Val | Val | Gly | Trp<br>190 | Arg | Gln | Glu | Leu | Arg<br>195 |   |   |     |      |   |   |   |
|      | Ala  | Tyr | Ala | Asp | Thr<br>200 | Lys | Leu | Ala | Asn | Val<br>205 | Leu | Phe | Ala | Arg | Glu<br>210 | 1 |   |     |      |   |   |   |
|      | Leu  | Ala | Asn | Gln | Leu<br>215 | Glu | Ala | Thr | Gly | Val<br>220 | Tḥr | Cys | Tyr | Ala | Ala<br>225 |   |   |     |      |   |   |   |
|      | His  | Pro | Gly | Pro | Val<br>230 | Asn | Ser | Glu | Leu | Phe<br>235 | Leu | Arg | His | Val | Pro<br>240 |   |   |     |      |   |   |   |
|      | Gly  | Trp | Leu | Arg | Pro<br>245 | Leu | Leu | Arg | Pro | Leu<br>250 | Ala | Trp | Leu | Val | Leu<br>255 | • |   |     |      |   |   |   |
|      | Arg  | Ala | Pro | Arg | Gly<br>260 |     | Ala | Gln | Thr | Pro<br>265 |     | Tyr | Cys | Ala | Leu<br>270 |   |   |     |      |   |   | • |
|      | Gln  | Glu | Gly | Ile | Glu<br>275 | Pro | Leu | Ser | Gly | Arg<br>280 |     | Phe | Ala | Asn | Cys<br>285 |   |   |     |      |   |   |   |
|      | His  | Val | Glu | Glu | Val<br>290 |     | Pro | Ala | Ala | Arg<br>295 |     | Asp | Arg | Ala | Ala<br>300 |   |   |     |      |   |   |   |
|      | His  | Arġ | Leu | Trp | Glu<br>305 |     | Ser | Lys | Arg | Leu<br>310 |     | Gly | Leu | Gly | Pro<br>315 |   |   |     |      |   |   |   |
|      | ·Gly | Glu | Asp | Ala | Glu<br>320 |     | Asp | Glu | Asp | Pro<br>325 |     | Ser | Glu | Asp | Ser<br>330 | • |   |     |      |   |   |   |
|      | Glu  | Ala | Pro | Ser | Ser<br>335 |     | Ser | Thr | Pro | His<br>340 |     | Glu | Glu | Pro | Thr<br>345 |   |   |     |      |   |   |   |
|      | Val  | Ser | Gln | Pŗo | Tyr<br>350 |     | Ser | Pro | Gln | Ser<br>355 |     | Pro | Asp | Leu | Ser<br>360 |   |   |     |      |   |   |   |
|      |      |     |     |     |            |     |     |     |     |            |     |     |     |     |            |   |   |     |      |   |   |   |
|      |      |     |     |     |            |     |     |     |     |            |     |     |     |     |            |   |   |     |      |   |   |   |
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gcccctgage atggtgcccc cagacccaca ccacctcctg cctgatggga 250

cccttctgct gctacagccc cctgcccggg gacatgccca cgatggccag 300

Lys Met Thr His Arg Ile Gln Ala Lys Val Glu Pro Glu Ile Gln

gccctgtcca cagacctggg tgtctacaca tgtgaggcca gcaaccggct 350 tggcacggca gtcagcagag gcgctcggct gtctgtggct gtcctccggg 400 aggatttcca gatccagcct cgggacatgg tggctgtggt gggtgagcag 450 tttactctgg aatgtgggcc gccctggggc cacccagagc ccacagtctc 500 atggtggaaa gatgggaaac ccctggccct ccagcccgga aggcacacag 550 tgtccggggg gtccctgctg atggcaagag cagagaagag tgacgaaggg 600 acctacatgt gtgtggccac caacagcgca ggacataggg agagccgcgc 650 agcccgggtt tccatccagg agccccagga ctacacggag cctgtggagc 700 ttctggctgt gcgaattcag ctggaaaatg tgacactgct gaacccggat 750 cctgcagagg gccccaagcc tagaccggcg gtgtggctca gctggaaggt 800 cagtggccct gctgcgcctg cccaatctta cacggccttg ttcaggaccc 850 agactgcccc gggaggccag ggagctccgt gggcagagga gctgctggcc 900 ggctggcaga gcgcagagct tggaggcctc cactggggcc aagactacga 950 gttcaaagtg agaccatcct ctggccgggc tcgaggccct gacagcaacg 1000 tgctgctcct gaggctgccg gaaaaagtgc ccagtgcccc acctcaggaa 1050 gtgactctaa agcctggcaa tggcactgtc tttgtgagct gggtcccacc 1100 acctgctgaa aaccacaatg gcatcatccg tggctaccag gtctggagcc 1150 tgggcaacac atcactgcca ccagccaact ggactgtagt tggtgagcag 1200 acccagetgg aaatcgccac ccatatgcca ggeteetaet gegtgcaagt 1250 ggctgcagtc actggtgctg gagctgggga gcccagtaga cctgtctgcc 1300 tccttttaga gcaggccatg gagcgagcca cccaagaacc cagtgagcat 1350 ggtccctgga ccctggagca gctgagggct accttgaagc ggcctgaggt 1400 cattgccacc tgcggtgttg cactctggct gctgcttctg ggcaccgccg 1450 tgtgtatcca ccgccggcgc cgagctaggg tgcacctggg cccaggtctg 1500 tacagatata ccagtgagga tgccatccta aaacacagga tggatcacag 1550 tgactcccag tggttggcag acacttggcg ttccacctct ggctctcggg 1600 acctgagcag cagcagcagc ctcagcagtc ggctgggggc ggatgcccgg 1650 gacccactag actgtcgtcg ctccttgctc tcctgggact cccgaagccc 1700

eggegtgeee etgetteeag acaccageae tttttatgge teeeteateg 1750 ctgagetgee etccagtace ecagecagge caagteecca ggteecaget 1800 gtcaggcgcc tcccacccca gctggcccag ctctccagcc cctgttccag 1850 ctcagacage ctctgcagee geaggggact ctcttctccc egettgtete 1900 tggcccctgc agaggcttgg aaggccaaaa agaagcagga gctgcagcat 1950 gccaacagtt ccccactget ccggggcagc cactccttgg agctccgggc 2000 ctgtgagtta ggaaatagag gttccaagaa cctttcccaa agcccaggag 2050 ctgtgcccca agctctggtt gcctggcggg ccctgggacc gaaactcctc 2100 ageteeteaa atgagetggt taetegteat eteeeteeag caeceetett 2150 tecteatgaa acteeceeaa eteagagtea acagaeeeag eeteeggtgg 2200 caccacagge teceteetee atcetgetge cagcageece catececate 2250 cttageccet gcagtecece tagececcag geetetteee tetetggeee 2300 cageceaget tecagtegee tgtecagete etcaetgtea tecetggggg 2350 aggatcaaga cagcgtgctg acccctgagg aggtagccct gtgcttggaa 2400 ctcagtgagg gtgaggagac tcccaggaac agcgtctctc ccatgccaag 2450 ggctccttca cccccacca cctatgggta catcagcgtc ccaacagcct 2500 cagagttcac ggacatgggc aggactggag gaggggtggg gcccaagggg 2550 ggagtettge tgtgeecace teggeeetge etcaceeca eccecagega 2600 gggctcctta gccaatggtt ggggctcagc ctctgaggac aatgccgcca 2650 gegeeagage cageettgte ageteeteeg atggeteett eetegetgat 2700 gctcactttg cccgggccct ggcagtggct gtggatagct ttggtttcgg 2750 tetagagece agggaggeag actgegtett catagatgee teateacete 2800 cctccccacg ggatgagate ttcctgaccc ccaacctctc cctgcccctg 2850 tgggagtgga ggccagactg gttggaagac atggaggtca gccacaccca 2900 geggetggga agggggatge etecetggee eeetgaetet eagatetett 2950 cccagagaag tcagctccac tgtcgtatgc ccaaggctgg tgcttctcct 3000 gtagattact cctgaaccgt gtccctgaga cttcccagac gggaatcaga 3050 accaettete etgteeacce acaagacetg ggetgtggtg tgtgggtett 3100 ggcctgtgtt tctctgcagc tggggtccac cttcccaagc ctccagagag 3150

|   | tt   | ctcc                                    | ctcc                                 | acga                     | attgi   | iga a                           | aaac                            | aaat                     | ga a                     | aacaa   | aaatt               | aga                             | agcaa                   | agc                             | 3200   |
|---|--|---|--------------------------------------|--------------------------|---|---------------------------------|---------------------------------|--------------------------|--------------------------|---|---------------------|---------------------------------|-------------------------|---------------------------------|--|
|   | tg   | acct                                    | ggag                                 | ccct                     | cago  | gga (                           | gcaaa                           | aacat                    | c a                      | tctc  | cacct               | gac                             | tcct                    | agc                             | 3250   |
|   | ca   | ctgc                                    | tttc                                 | tcct                     | ctgt  | gc (                            | catco                           | cacto                    | cc ca                    | accad   | ccago               | tto                             | jtttt                   | ggc                             | 3300   |
|   |  |   |                                      |                          |   |                                 |                                 |                          |                          |   |                     |                                 |                         |                                 | 3350   |
|   | aaq  | gtgga                                   | agga                                 | gcca                     | gago  | gtg d                           | cctt                            | gtg                      | ga go                    | gacaç   | cagt                | ggc                             | tgct                    | ggg                             | 3400   |
|   | aga  | aggg                                    | ctgt                                 | ggag                     | gaag  | ga q                            | gctto                           | ctcgc                    | ja go                    | cccc  | tctc                | ago                             | ctta                    | cct                             | 3450   |
|   | ggg  | gece                                    | ctcc                                 | tcta                     | igaga   | ag a                            | gcto                            | caact                    | c to                     | ctccc   | aacc                | tca                             | ccat                    | gga                             | 3500   |
|   | aaq  | gaaaa                                   | ataa                                 | ttat                     | gaat  | gc c                            | acto                            | gaggo                    | a ct                     | gagg  | ccct                | acc                             | tcat                    | gcc                             | 3550   |
|   | aaa  | caaa                                    | ggg                                  | ttca                     | aggo  | tg c                            | gtct                            | agcg                     | ra go                    | gatgo   | tgaa                | .gga                            | aggg                    | agg_                            | 3600   |
|   | tat  | gaga                                    | ccg                                  | tagg                     | tcaa  | aa g                            | cacc                            | atco                     | t co                     | tact  | gttg                | tca                             | ctat                    | gag                             | 3650   |
|   | ctt  | aaga                                    | aat                                  | ttga                     | tacc  | at a                            | aaat                            | ggta                     | a aa                     | ıaaaa   | aaaa                | aaa                             | aaaa                    | aaa                             | 3700   |
|   | aaa  | aaaa                                    | aaa                                  | aaaa                     | aa 3  | 716                             |                                 |                          |                          |   | ·                   |                                 |                         |                                 |  |
| < | 211<br>212                                   | > 21<br>> 98<br>> PR<br>> Ho            | 5<br>T                               | ani a                    | n.e   | *                               |                                 |                          | 3)                       |   |                     |                                 |                         |                                 |  |
| ` | 213  | - 110                                   | mo s                                 | abre                     | 113   |                                 |                                 |                          |                          |   |                     |                                 |                         |                                 |  |
| < | :.<br>400                                    | > 21                                    | 1                                    |                          |   |                                 | •                               |                          | 1 0                      | 2   |                     | i.                              |                         |                                 |  |
| < | :.<br>400                                    | > 21                                    | 1                                    |                          |   | Gln                             | Asp                             | Ser                      | Pro                      | Pro<br>10   | Gln                 | Ile                             | Leu                     | Val                             | His<br>15  |
| < | 400<br>Met<br>1                              | > 21<br>Gly                             | 1<br>Gly                             | Met                      | Ala<br>5  | Phe                             |                                 |                          | :                        | . 10  |                     | 6 .                             |                         | 7                               |  |
| < | 400<br>Met<br>1<br>Pro                       | > 21<br>Gly<br>Gln                      | 1<br>Gly<br>Asp                      | Met                      | Ala<br>5<br>Leu<br>20                           | Phe                             | Gln                             | Gly                      | Pro                      | 10<br>Gly<br>25   | Pro                 | Ala                             | ,<br>Arg                | Met                             | 15<br>Ser  |
|   | 400<br>Met<br>1<br>Pro<br>Cys                | > 21<br>Gly<br>Gln                      | 1<br>Gly<br>Asp<br>Ala               | Met<br>Gln<br>Ser        | Ala<br>5<br>Leu<br>20<br>Gly<br>35              | Phe                             | Gln<br>Pro                      | Gly<br>Pro               | Pro                      | 10<br>Gly<br>25<br>Thr<br>40  | Pro                 | Ala<br>Arg                      | Arg<br>Trp              | Met<br>Leu                      | Ser<br>30  |
|   | 400<br>Met<br>1<br>Pro<br>Cys                | > 21<br>Gly<br>Gln<br>Gln               | l<br>Gly<br>Asp<br>Ala<br>Gln        | Met<br>Gln<br>Ser        | Ala<br>5<br>Leu<br>20<br>Gly<br>35<br>Leu<br>50 | Phe<br>Gln<br>Ser               | Gln<br>Pro<br>Met               | Gly<br>Pro<br>Val        | Pro<br>Pro               | 10<br>Gly<br>25<br>Thr<br>40<br>Pro<br>55                           | Pro<br>Ile<br>Asp   | Ala<br>Arg<br>Pro               | Arg<br>Trp              | Met<br>Leu<br>His               | 15<br>Ser<br>30<br>Leu<br>45<br>Leu<br>60                            |
|   | 400<br>Met<br>1<br>Pro<br>Cys<br>Asn         | > 21<br>Gly<br>Gln<br>Gln<br>Fro        | 1<br>Gly<br>Asp<br>Ala<br>Gln<br>Asp | Met<br>Gln<br>Ser<br>Pro | Ala 5 Leu 20 Gly 35 Leu 50 Thr 65               | Phe<br>Gln<br>Ser<br>Leu        | Gln<br>Pro<br>Met<br>Leu        | Gly<br>Pro<br>Val<br>Leu | Pro Pro Leu              | 10<br>Gly<br>25<br>Thr<br>40<br>Pro<br>55<br>Gln<br>70              | Pro Ile Asp         | Ala<br>Arg<br>Pro               | Arg<br>Trp<br>His       | Met<br>Leu<br>His               | 15<br>Ser<br>30<br>Leu<br>45<br>Leu<br>60                            |
|   | 400<br>Met<br>1<br>Pro<br>Cys<br>Asn<br>Leu  | > 21<br>Gly<br>Gln<br>Gln<br>Pro        | l<br>Gly<br>Asp<br>Ala<br>Gln<br>Asp | Met Gln Ser Pro Gly      | Ala 5 Leu 20 Gly 35 Leu 50 Thr 65 Gly 80        | Phe<br>Gln<br>Ser<br>Leu<br>Gln | Gln<br>Pro<br>Met<br>Leu<br>Ala | Gly<br>Pro<br>Val<br>Leu | Pro Pro Leu              | 10<br>Gly<br>25<br>Thr<br>40<br>Pro<br>55<br>Gln<br>70<br>Thr<br>85 | Pro Ile Asp Pro Asp | Ala<br>Arg<br>Pro<br>Pro        | Arg Trp His Ala Gly     | Met<br>Leu<br>His<br>Arg        | 15<br>Ser<br>30<br>Leu<br>45<br>Leu<br>60<br>Gly<br>75<br>Tyr<br>90  |
|   | 4000<br>Met<br>1<br>Pro<br>Cys<br>Asn<br>Leu | > 21<br>Gly<br>Gln<br>Gln<br>Pro<br>Ala | l<br>Gly<br>Asp<br>Ala<br>Gln<br>Asp | Met Gln Ser Pro Gly Asp  | Ala 5 Leu 20 Gly 35 Leu 50 Thr 65 Gly 80 Ser 95 | Phe<br>Gln<br>Ser<br>Leu<br>Gln | Gln<br>Pro<br>Met<br>Leu<br>Ala | Gly Pro Val Leu Leu      | Pro<br>Pro<br>Leu<br>Ser | 10<br>Glyy25<br>Thr 40<br>Pro 55<br>Gln 70<br>Thr 85<br>Thr 100     | Pro Ile Asp Pro Asp | Ala<br>Arg<br>Pro<br>Pro<br>Leu | Arg Trp His Ala Gly Ser | Met<br>Leu<br>His<br>Arg<br>Val | Ser<br>30<br>Leu<br>45<br>Leu<br>60<br>Gly<br>75<br>Tyr<br>90<br>Gly |

|   | Cys | Gly | Pro | Pro     | Trp<br>140 | Gly | His | Pro | Glu | Pro<br>145 | Thr | Val | Ser | Trp | Trp<br>150  |                  |   |      |      |  |
|---|-----|-----|-----|---------|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|-------------|------------------|---|------|------|--|
|   | Lys | Asp | Gly | Lys     | Pro<br>155 | Leu | Ala | Leu | Gln | Pro<br>160 | Gly | Arg | His | Thr | Val<br>165  |                  |   |      |      |  |
|   | Ser | Gly | Gly | Ser     | Leu<br>170 | Leu | Met | Ala | Arg | Ala<br>175 | Glu | Lys | Ser | Asp | Glu<br>180  |                  |   |      |      |  |
|   | Gly | Thr | Tyr | Met     | Cys<br>185 | Val | Ala | Thr | Asn | Ser<br>190 | Ala | Gly | His | Arg | Glu<br>195  |                  |   |      |      |  |
|   | Ser | Arg | Ala | Ala     | Arg<br>200 |     | Ser | Ile | Gln | Glu<br>205 | Pro | Gln | Asp | Tyr | Thr<br>210  |                  |   |      |      |  |
|   | Glu | Pro | Val | Glu<br> | Leu<br>215 | Leu |     |     |     |            | Gln |     |     | Asn |             | a was made state | - | <br> | <br> |  |
|   | Thr | Leu | Leu | Asn     | Pro<br>230 | Asp | Pro | Ala | Glu | Gly<br>235 | Pro | Lys | Pro | Arg | Pro<br>240  |                  |   |      |      |  |
|   | Ala | Val | Trp | Leu     | Ser<br>245 | Trp | Lys | Val | Ser | Gly<br>250 | Pro | Ala | Ala | Pro | Ala<br>255  |                  |   |      |      |  |
|   |     |     |     |         | 260        |     |     |     |     | 265        |     |     |     | Gly | 270         |                  |   |      | •    |  |
|   |     | Ī   | •   |         | 275        | ٠   |     |     |     | 280        |     | . – | -   |     | Ser.<br>285 |                  |   |      | ٠    |  |
|   |     |     |     |         | 290        |     |     | ٠.  |     | 295        |     |     |     | Phe | 300         | . •              |   |      |      |  |
|   | •   |     |     |         | 305        |     |     |     |     | 310        |     |     |     | Asn | 315         |                  |   |      |      |  |
|   |     |     |     |         | 320        |     |     |     |     | 325        |     |     |     | Pro | 330         |                  |   |      |      |  |
|   |     |     |     |         | 335        |     |     |     |     | 340        |     |     |     | Ser | 345         |                  |   |      |      |  |
|   |     |     |     |         | 350        |     |     |     |     | 355        |     |     |     | Gly | 360         |                  |   |      |      |  |
|   |     |     |     |         | 365        |     |     |     |     | 370        |     |     |     | Asn | 375         |                  |   |      |      |  |
| • | -   |     |     |         | 380        |     |     |     |     | 385        |     |     |     | His | 390         |                  |   |      |      |  |
|   |     |     |     |         | 395        |     |     |     |     | 400        |     |     | •   |     | Gly 405     |                  |   |      | •    |  |
|   | Ala | GTÀ | GIU | Pro     | 410        | Arg | rro | val | cys | 415        |     | ьeu | GIU | Gln | 420         |                  |   |      |      |  |

|    | Met   | Glu | Arg | Ala | Thr<br>425 |     | Glu              | Pro | Ser | Glu<br>430 | His | Gly | Pro | Trp | Thr<br>435  |   |  |   |   |   |          |   |
|----|-------|-----|-----|-----|------------|-----|------------------|-----|-----|------------|-----|-----|-----|-----|-------------|---|--|---|---|---|----------|---|
|    | Leu   | Glu | Gln | Leu | Arg<br>440 | Ala | Thr              | Leu | Lys | Arg<br>445 | Pro | Glu | Val | Ile | Ala<br>450  |   |  |   |   |   |          |   |
|    | Thr   | Cys | Gly | Val | Ala<br>455 | Leu | Trp              | Leu | Leu | Leu<br>460 | Leu | Gly | Thr | Ala | Val<br>465  |   |  |   | ٠ |   |          |   |
|    | Cys   | Ile | His | Arg | Arg<br>470 | Arg | Arg              | Ala | Arg | Val<br>475 | His | Leu | Gly | Pro | Gly<br>480  |   |  |   |   |   |          |   |
|    | · Leu | Tyr | Arg | Tyr | Thr<br>485 |     | Glu              | Asp | Ala | Ile<br>490 | Leu | Lys | His | Arg | Met<br>495  |   |  |   |   |   |          |   |
|    | Asp   | His | Ser | Asp | Ser<br>500 | Gln | Trp              | Leu | Ala | Asp<br>505 |     |     |     |     | Thr<br>510_ | · |  |   |   |   | <u>-</u> |   |
|    | Ser   | Gly | Ser | Arg | Asp<br>515 | Leu | Ser              | Ser | Ser | Ser<br>520 | Ser | Leu | Ser | Ser | Arg<br>525  |   |  |   |   | , |          |   |
| ٠. | Leu   | Gly | Ala | Asp | Ala<br>530 | Arg | Asp              | Pro | Leu | Asp<br>535 | Cys | Arg | Arg | Ser | Leu<br>540  |   |  |   | • |   |          |   |
| ÷  | Leu   | Ser | Trp | Asp |            | Arg |                  | Pro | Gly | Val<br>550 | Pro | Leu | Leu | Pro | Asp<br>555  | • |  | , |   |   |          |   |
|    | Thr   | Ser | Thr | Phe | Tyr<br>560 |     | Ser              | Leu | Ile | Ala<br>565 | Glu | Leu | Pro | Ser | Ser<br>570  |   |  |   |   |   |          |   |
|    | Thr   | Pro | Ala | Arg | Pro<br>575 | Ser | Pro              | Gln | Val | Pro<br>580 |     | Val | Arg | Arg | Leu<br>585  |   |  |   |   |   |          |   |
|    | Pro   | Pro | Gln | Leu | Ala<br>590 |     | Leu              | Ser | Ser | Pro<br>595 |     | Ser | Ser | Ser | Asp<br>600  |   |  |   |   |   |          |   |
|    | Ser   | Leu | Cys | Ser | Arg<br>605 |     | <sub>-</sub> Gly | Leu | Ser | Ser<br>610 | Pro | Arg | Leu | Ser | Leu<br>615  |   |  |   |   |   |          |   |
|    | Ala   | Pro | Ala | Glu | Ala<br>620 | _   | Lys              | Ala | Lys | Lys<br>625 |     | Gln | Glu | Leu | Gln<br>630  |   |  |   |   |   |          |   |
|    | His   | Ala | Asn | Ser | Ser<br>635 | Pro | Leu              | Leu | Arg | Gly<br>640 |     | His | Ser | Leu | Glu<br>645  |   |  |   |   |   |          | i |
|    | Leu   | Arg | Ala | Суѕ | Glu<br>650 |     | Gly              | Asn | Arg | Gly<br>655 |     | Lys | Asn | Leu | Ser<br>660  |   |  |   |   |   |          |   |
|    | Gln   | Ser | Pro | Gly | Ala<br>665 |     | Pro              | Gln | Ala | Leu<br>670 |     | Ala | Trp | Arg | Ala<br>675  |   |  |   |   |   |          |   |
|    | Lev   | Gly | Pro | Lys | Leu<br>680 |     | Ser              | Ser | Ser | Asn<br>685 |     | Leu | Val | Thr | Arg<br>690  |   |  |   |   |   | *        |   |
|    | His   | Leu | Pro | Pro | Ala<br>695 |     | Leu              | Phe | Pro | His<br>700 |     | Thr | Pro | Pro | Thr<br>705  |   |  |   |   |   |          |   |
|    |       |     |     |     |            |     |                  |     |     |            |     |     |     |     |             |   |  |   |   |   |          |   |

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|                                       |     |       |     |     |            |     |     |     |     |                  |     | •   |     |     |             |   |   | ٠. |   |              |     |     |    |
|---------------------------------------|-----|-------|-----|-----|------------|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-------------|---|---|----|---|--------------|-----|-----|----|
| :                                     |     |       |     |     |            |     |     |     |     |                  |     |     |     |     | •           |   |   |    |   |              | •   |     |    |
| II.                                   |     |       |     |     |            |     |     |     |     |                  |     |     |     |     |             |   |   |    |   |              |     |     | •  |
|                                       | Glr | Ser   | Gln | Gln | Thr<br>710 | Gln | Pro | Pro | Val | Ala <sup>.</sup> | Pro | Gln | Ala | Pro | Ser<br>720  | • |   |    |   |              |     |     |    |
| ·<br>=                                | Ser | Ile   | Leu | Leu |            | Ala | Ala | Pro | Ile | •                | Ile | Leu | Ser | Pro | Cys<br>735  |   |   |    |   |              |     |     |    |
|                                       | Ser | Pro   | Pro | Ser | Pro<br>740 | Gln | Ala | Ser | Ser | Leu<br>745       | Ser | Gly | Pro | Ser | Pro<br>750  |   |   |    |   |              |     | • . |    |
|                                       | Ala | Ser   | Ser | Arg | Leu<br>755 | Ser | Ser | Ser | Ser | Leu<br>760       | Ser | Ser | Leu | Gly | Glu<br>765  |   |   |    |   |              |     |     |    |
|                                       | Asp | Gln   | Asp | Ser | Val<br>770 | Leu | Thr | Pro | Glu | Glu<br>775       | Val | Ala | Leu | Cys | Leu<br>780  |   |   |    |   |              |     |     |    |
|                                       | Glu | Leu   | Ser | Glu |            |     |     |     |     |                  |     |     |     |     | Pro<br>795- |   |   |    |   | دونو د مشورو |     |     |    |
|                                       | Met | Pro   | Arg | Ala | Pro<br>800 | Ser | Pro | Pro | Thr | Thr<br>805       |     | Gly | Tyr | Ile | Ser<br>810  |   | · |    |   |              |     | •   |    |
|                                       | Val | l Pro | Thr | Ala | Ser<br>815 | Glu | Phe | Thr | Asp | Met<br>820       | Gly | Arg | Thr |     | Gly<br>825  | , |   |    |   |              |     |     |    |
|                                       | Gly | / Val | Gly | Pro | Lys<br>830 | Gly | Gly | Val | Leu | Leu<br>835       | Cys | Pro | Pro | Arg | Pro<br>840  |   |   |    |   |              | . ' |     |    |
|                                       | Cys | Leu   | Thr | Pro | Thr<br>845 | Pro | Ser | Glu | Gly | Ser<br>850       | Leu | Ala | Asn | Gly | Trp<br>855  |   |   |    |   |              |     |     |    |
|                                       | Gly | y Ser | Ala | Ser | Glu<br>860 |     | Asn | Ala | Ala | Ser<br>865       |     | Arg | Ala | Ser | Leu<br>870  |   | , |    |   |              |     |     |    |
| · × ·                                 | Va  | l Ser | Ser | Ser | Asp<br>875 |     | Ser | Phe | Leu | Ala<br>880       |     | Ala | His | Phe | Ala<br>885  |   |   |    |   |              |     | ·   |    |
|                                       | Arg | g Ala | Leu |     | Val<br>890 | Ala | Val | Asp | Ser | Phe<br>895       |     | Phe | Gly | Leu | Glu<br>900  |   |   |    |   |              |     |     |    |
|                                       | Pro | Arg   | Glu | Āla | Asp<br>905 | Cys | Val | Phe | Ile | Asp<br>910       |     | Ser | Ser | Pro | Pro<br>915  |   |   |    |   | a e          |     | ÷ . | ,  |
|                                       | Se  | r Pro | Arg | Asp | Glu<br>920 |     | Phe | Leu | Thr | Pro<br>925       |     | Leu | Ser | Leu | Pro<br>930  |   | • |    |   |              |     |     |    |
|                                       | Le  | ı Trp | Glu | Trp | Arg<br>935 | Pro | Asp | Trp | Leu | Glu<br>940       |     | Met | Glu | Val | Ser<br>945  |   |   |    |   |              |     |     | ē  |
| · · · · · · · · · · · · · · · · · · · | His | s Thr | Gln | Arg | Leu<br>950 |     | Arg | Gly | Met | Pro<br>955       |     | Trp | Pro | Pro | 960         | • |   | ٠. |   |              |     | -   |    |
|                                       | Se  | r Gln | Ile |     | Ser<br>965 |     | Arg | Ser | Gln | Leu<br>970       |     | Cys | Arg | Met | Pro<br>975  | • |   |    | • |              |     |     |    |
|                                       | Ly  | s Alạ | Gly | Ala | Ser<br>980 |     | Val | Asp | Tyr | Ser<br>985       |     |     |     |     |             |   |   |    |   |              |     |     |    |
|                                       |     |       |     |     | 8.         |     |     |     |     |                  |     |     |     |     |             |   |   |    |   |              |     |     | •. |
| , .                                   |     |       |     |     |            |     |     |     |     |                  |     |     | •   |     |             |   |   |    |   |              |     |     |    |

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Asp Thr Val Ser Leu Gln Cys Thr Tyr Arg Glu Glu Leu Arg Asp 35 40 45

His Arg Lys Tyr Trp Cys Arg Lys Gly Gly Ile Leu Phe Ser Arg

50 55 60

| Cys | Ser  | Gly   | Thr  | Ile<br>65   | Tyr  | Ala | Glu  | Glu | Glu<br>70  | Gly | Gln | Glu | Thr | Met<br>75  |
|-----|------|-------|------|-------------|------|-----|------|-----|------------|-----|-----|-----|-----|------------|
| Lys | Gly  | Arg   | Val  | Ser<br>80   | Ile  | Arg | Asp  | Ser | Arg<br>85  | Gln | Glu | Leu | Ser | Leu<br>90  |
| Ile | Val  | Thr   | Leu  | Trp<br>95   | Asn  | Leu | Thr  | Leu | Gln<br>100 | Asp | Ala | Gly | Glu | Tyr<br>105 |
| Trp | Cys  | Gly   | Val  | Glu<br>110  | Lys  | Arg | Gly  | Pro | Asp<br>115 | Glu | Ser | Leu | Leu | Ile<br>120 |
| Ser | Leu  | Phe   | Val  | Phe<br>125  | Pro  | Gly | Pro  | Cys | Cys<br>130 |     | Pro | Ser | Pro | Ser<br>135 |
| Pro | -Thr | -Phe- | -Gln | -Pro<br>140 | Leu- | Ala | -Thr | Thr | Arg<br>145 | Leu | Gln | Pro | Lys | Ala<br>150 |
| Lys | Ala  | Gln   | Gln  | Thr<br>155  | Gln  | Pro | Pro  | Gly | Leu<br>160 | Thr | Ser | Pro | Gly | Leu<br>165 |
| Tyr | Pro  | Ala   | Ala  | Thr<br>170  | Thr  | Ala | Lys  | Gln | Gly<br>175 | Lys | Thr | Gly | Ala | Glu<br>180 |
| Ala | Pro  | Pro   | Leu  | Pro<br>185  | Gly  | Thr | Ser  | Gln | Tyr<br>190 | Gly | His | Glu | Arg | Thr<br>195 |
| Ser | Gľn  | Tyr   | Thr  | Gly<br>200  | Thr  | Ser | Pro  | His | Pro<br>205 | Ala | Thr | Ser | Pro | Pro<br>210 |
| Ala | Gly  | Ser   | Ser  | Arg<br>215  | Pro  | Pro | Met  | Gln | Leu<br>220 | Asp | Ser | Thr | Ser | Ala<br>225 |
| Glu | Asp  | Thr   | Ser  | Pro<br>230  | Ala  | Leu | Ser  | Ser | Gly<br>235 | Ser | Ser | Lys | Pro | Arg<br>240 |
| Val | Ser  | Ile   | Pro  | Met<br>245  | Val  | Arg | Ile  | Leu | Ala<br>250 |     | Val | Leu | Val | Leu<br>255 |
| Leu | Ser  | Leu   | Leu  | Ser<br>260  | Ala  | Ala | Gly  | Leu | Ile<br>265 | Ala | Phe | Суѕ | Ser | His<br>270 |
| Leu | Leu  | Leu   | Trp  | Arg<br>275  | Lys  | Glu | Ala  | Gln | Gln<br>280 | Ala | Thr | Glu | Thr | Gln<br>285 |
| Arg | Asn  | Glu   | Lys  | Phe<br>290  | Trp  | Leu | Ser  | Arg | Leu<br>295 |     | Ala | Glu | Glu | Lys<br>300 |
| Glu | Ala  | Pro   | Ser  | Gln<br>305  |      | Pro | Glu  | Gly | Asp<br>310 |     | Ile | Ser | Met | Pro<br>315 |
| Pro | Leu  | His   | Thr  | Ser<br>320  |      | Glu | Glu  | Leu | Gly<br>325 |     | Ser | Lys | Phe | Val<br>330 |
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His Asp Phe Gly Leu Asp Gly Tyr Arg Gly Tyr Ser Leu Ala Asp
35
40

Trp Val Cys Leu Ala Tyr Phe Thr Ser Gly Phe Asn Ala Ala 50 55 60

Leu Asp Tyr Glu Ala Asp Gly Ser Thr Asn Asn Gly Ile Phe Gln
65 70 75

Ile Asn Ser Arg Arg Trp Cys Ser Asn Leu Thr Pro Asn Val Pro  $80 \hspace{1cm} 85 \hspace{1cm} 90$ 

Asn Val Cys Arg Met Tyr Cys Ser Asp Leu Leu Asn Pro Asn Leu 95 100 105

Lys Asp Thr Val Ile Cys Ala Met Lys Ile Thr Gln Glu Pro Gln 110 115 120

Gly Leu Gly Tyr Trp Glu Ala Trp Arg His His Cys Gln Gly Lys 125 130 135

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<213> Homo sapiens

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35 40 45

Leu Lys Gly Leu Ile Gln Arg Gln Val Gln Met Cys Lys Arg Asn 50 55 60

Leu Glu Val Met Asp Ser Val Arg Arg Gly Ala Gln Leu Ala Ile 65 70 75

Glu Glu Cys Gln Tyr Gln Phe Arg Asn Arg Arg Trp Asn Cys Ser 80 85 90

Thr Leu Asp Ser Leu Pro Val Phe Gly Lys Val Val Thr Gln Gly 95 100 105

Thr Arg Glu Ala Ala Phe Val Tyr Ala Ile Ser Ser Ala Gly Val 110 115 120

Ala Phe Ala Val Thr Arg Ala Cys Ser Ser Gly Glu Leu Glu Lys 125 130 135

Cys Gly Cys Asp Arg Thr Val His Gly Val Ser Pro Gln Gly Phe 140 145 150

Gln Trp Ser Gly Cys Ser Asp Asn Ile Ala Tyr Gly Val Ala Phe 155 160 165

Ser Gln Ser Phe Val Asp Val Arg Glu Arg Ser Lys Gly Ala Ser 170 175 180

Ser Ser Arg Ala Leu Met Asn Leu His Asn Asn Glu Ala Gly Arg 185 190 195

Lys Ala Ile Leu Thr His Met Arg Val Glu Cys Lys Cys His Gly 200 205 210

Val Ser Gly Ser Cys Glu Val Lys Thr Cys Trp Arg Ala Val Pro

Pro Phe Arg Gln Val Gly His Ala Leu Lys Glu Lys Phe Asp Gly 230 Ala Thr Glu Val Glu Pro Arg Arg Val Gly Ser Ser Arg Ala Leu 245 250 Val Pro Arg Asn Ala Gln Phe Lys Pro His Thr Asp Glu Asp Leu 260 Val Tyr Leu Glu Pro Ser Pro Asp Phe Cys Glu Gln Asp Met Arg 275 Ser Gly Val Leu Gly Thr Arg Gly Arg Thr Cys Asn Lys Thr Ser 290 295 Lys Ala Ile Asp Gly Cys Glu Leu Leu Cys Cys Gly Arg Gly Phe 310 His Thr Ala Gln Val Glu Leu Ala Glu Arg Cys Ser Cys Lys Phe 320 His Trp Cys Cys Phe Val Lys Cys Arg Gln Cys Gln Arg Leu Val 335 Glu Leu His Thr Cys Arg 350 <210> 227 -<211> 23 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 227 gctgcagctg caaattccac tgg 23 <210> 228 <211> 28 <212> DNA <213> Artificial Sequence <223> Synthetic oligonucleotide probe <400> 228

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Pro Leu Phe Leu Ala Leu Ala Val Leu Val Thr Thr Val Leu Trp
35 40 45

Ala Val Ile Leu Ser Ile Leu Leu Ser Lys Ala Ser Thr Glu Arg
50 55 60

Ala Ala Leu Leu Asp Gly His Asp Leu Leu Arg Thr Asn Ala Ser
65 70 75

Lys Gln Thr Ala Ala Leu Gly Ala Leu Lys Glu Glu Val Gly Asp 80 85 90

Cys His Ser Cys Cys Ser Gly Thr Gln Ala Gln Leu Gln Thr Thr 95 100 105

Arg Ala Glu Leu Gly Glu Ala Gln Ala Lys Leu Met Glu Gln Glu
110 115 120

Ser Ala Leu Arg Glu Leu Arg Glu Arg Val Thr Gln Gly Leu Ala 125 130 135

Glu Ala Gly Arg Gly Arg Glu Asp Val Arg Thr Glu Leu Phe Arg 140 145 150

Ala Leu Glu Ala Val Arg Leu Gln Asn Asn Ser Cys Glu Pro Cys 155 160 165

Pro Thr Ser Trp Leu Ser Phe Glu Gly Ser Cys Tyr Phe Phe Ser 170 180

Val Pro Lys Thr Thr Trp Ala Ala Gln Asp His Cys Ala Asp 185 190 195

Ala Ser Ala His Leu Val Ile Val Gly Gly Leu Asp Glu Gln Gly 200 205 210

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Ser Asn Gly Leu Arg Asp Phe Ala Glu Arg Gly Glu Ala Trp Ala

Leu Met Lys Glu Ile Glu Ala Ala Gly Glu Ala Leu Gln Ser Val

His Glu Val Phe Ser Ala Pro Ala Val Pro Ser Gly Thr Gly Gln 125

Thr Ser Ala Glu Leu Glu Val Gln Arg Arg His Ser Leu Val Ser 140

Phe Val Val Arg Ile Val Pro Ser Pro Asp Trp Phe Val Gly Val 155

| •   | Asp Ser                                      | Leu Asp | Leu Cys<br>170 | Asp Gl   | y Asp | Arg<br>175   |     | Arg | Glu    | Gln     | Ala<br>180 |     |     |     |              |
|-----|--|---------|----------------|----------|-------|--------------|-----|-----|--------|---------|------------|-----|-----|-----|--------------|
| •   | Ala Leu                                      | Asp Leu | Tyr Pro<br>185 | Tyr Ası  | o Ala | Gly<br>190   |     | Asp | Ser    | Gly     | Phe<br>195 |     |     |     |              |
|     | Thr Phe                                      | Ser Ser | Pro Asn<br>200 | Phe Ala  | a Thr | Ile<br>205   |     | Gln | Asp    | Thr     | Val<br>210 |     |     |     |              |
|     | Thr Glu                                      | Ile Thr | Ser Ser<br>215 | Ser Pr   | o Ser | His<br>220   |     | Ala | Asn    | Ser     | Phe<br>225 |     |     |     |              |
| Ť   | Tyr Tyr                                      | Pro Arg | Leu Lys<br>230 | Ala Le   | u Pro | Pro<br>235   |     | Ala | Arg    | Val     | Thr<br>240 |     |     |     | . <u>.</u> . |
|     | Leu Leu                                      | Arg Leu | Arg Gln        | Ser Pr   | o Arg | Ala<br>250   | Phe | Ile | Pro    | Pro<br> | Ala<br>255 |     |     | ÷   | 1            |
|     | Pro Val                                      | Leu Pro | Ser Arg<br>260 | Asp As   | n Glu | 11e<br>265   |     | Asp | Ser    | Ala     | Ser<br>270 |     |     |     |              |
| *   | Val Pro                                      | Glu Thr | Pro Leu<br>275 | Asp Cy   | s Glu | Val<br>280   |     | Leu | Trp    | Ser     | Ser<br>285 | ÷ . |     |     |              |
|     | Trp Gly                                      | Leu Cys | Gly Gly<br>290 | His Cy   | s Gly | / Arg<br>295 |     | Gly | Thr    | Lys     | Ser<br>300 |     | *   |     |              |
| •   | Arg Thr                                      | Arg Tyr | Val Arg        | Val Gl   | n Pro | Ala<br>310   |     | Asn | Gly    | Ser     | Pro<br>315 |     |     | **  |              |
|     | Cys Pro                                      | Glu Lev | Glu Glu<br>320 | Glu Al   | a Glu | 1 Cys<br>325 |     | Pro | Asp    | Asn     | Cys<br>330 |     |     |     | · •.         |
|     | Val  |         | *<br>*         |          |       |              | a.  |     |        |         | : .        |     | · . |     | ÷            |
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|     | <400> 23<br>cagcact                          |         | ggaagag g      | ıg 22    |       |              |     |     |        | •       |            |     |     |     |              |
| - 8 | <210> 23<br><211> 18<br><212> DN<br><213> Ar | B<br>IA | l Sequenc      | ce       |       |              |     | : . |        |         |            |     |     |     |              |
|     | <220><br><223> Sy                            | nthetic | oligonud       | cleotide | pro   | be           |     |     |        |         |            |     | •   |     |              |
|     | <400>.23<br>caggact                          |         | gtccg 18       |          |       |              |     |     |        | •       |            |     | •   |     |              |
| 4   |  | , ·     |                | ٠        |       |              |     |     | •<br>n | •       |            | •   |     |     |              |
|     |  |         | . •            |          |       |              | ,   |     |        |         |            |     |     |     | •            |

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Glu Ala Tyr Tyr Asp Asn Thr Ile Phe His Arg Val Val Pro Gly 50 55 60

Phe Ile Val Gln Gly Gly Asp Pro Thr Gly Thr Gly Ser Gly Gly 65 70 75

Glu Ser Ile Tyr Gly Ala Pro Phe Lys Asp Glu Phe His Ser Arg

Leu Arg Phe Asn Arg Arg Gly Leu Val Ala Met Ala Asn Ala Gly 95 100 105

Ser'His Asp Asn Gly Ser Gln Phe Phe Phe Thr Leu Gly Arg Ala 110 115 120

Asp Glu Leu Asn Asn Lys His Thr Ile Phe Gly Lys Val Thr Gly 125 130 135

|                   | Asp ( | Thr | Val | Tyr | Asn<br>140 | Met  | Leu  | Arg | Leu   | Ser<br>145 | Glu | Val | Asp | Ile  | Asp<br>150              |   |        |     |    | ٠   |   |
|-------------------|-------|-----|-----|-----|------------|------|------|-----|-------|------------|-----|-----|-----|------|-------------------------|---|--------|-----|----|-----|---|
|                   | Asp i | Asp | Glu | Arg | Pro<br>155 | His  | Asn  | Pro | His   | Lys<br>160 | Ile | Lys | Ser | Cys  | Glu<br>165              |   |        |     |    |     |   |
|                   | Val : | Leu | Phe | Asn | Pro<br>170 | Phe  | Asp  | Asp | Ile   | Ile<br>175 | Pro | Arg | Glu | Ile  | Lys<br>180              |   |        |     |    |     |   |
|                   | Arg : | Leu | Lys | Lys | Glu<br>185 | Lys  | Pro  | Glu | Glu   | Glu<br>190 | Val | Lys | Lys | Leu  | Lys<br>195              |   |        |     |    |     |   |
|                   | Pro   | Lys | Gly |     | Lys<br>200 | Asn  | Phe  | Ser | Leu   | Leu<br>205 | Ser | Phe | Gly | Glu  | Glu<br>210              | • |        | •   |    |     |   |
| » <del>:-</del> - | Ala   |     |     |     |            |      |      |     |       |            |     |     |     |      | Met<br>225-             |   | نسب سد |     |    |     |   |
| •                 | Lys   | Gly | Lys | Ser | Lys<br>230 | Ser. | Ser  | His | Asp   | Leu<br>235 | Leu | Lys | Asp | Asp  | Pro<br>240              |   |        |     |    |     |   |
|                   | His   | Leu | Ser | Ser | Val<br>245 | Pro  | Val  | Val | Glu   | Ser<br>250 | Glu | Lys | Gly | Asp  | Ala<br>255              |   |        |     |    |     |   |
|                   | Pro.  | Asp | Leu | Val | Asp<br>260 | Asp  | Gly. | Glu | Asp   | Glu<br>265 | Ser | Ala | Glu | His  | Asp<br>270              |   |        |     | ŧ  |     | , |
| •                 | Glu   | Tyr | Ile | Asp | Gly<br>275 | Asp  | Glu  | Lys | Asn   | Leu<br>280 | Met | Arg | Glu | Arg  | Ile <sup>.</sup><br>285 |   |        |     |    |     |   |
|                   | Ala   | Lys | Lys | Leu | Lys<br>290 | Lys  | Asp  | Thr | Ser   | Ala<br>295 | Asn | Val | Lys | 'Ser | Ala<br>300              |   |        | , . |    |     |   |
| *                 | Gly   | Glu | Gly | Glu | Val<br>305 | Glu  | Lys  | Lys | Ser   | Val<br>310 | Ser | Arg | Ser | Glu  | Glu<br>315              |   |        |     |    |     |   |
|                   | Leu   | Arg | Lys | Glu | Ala<br>320 | Arg  | Gln  | Leu | Lys   | Arg<br>325 | Glu | Leu | Leu | Ala  | Ala<br>330              |   |        |     |    |     |   |
|                   | Lys   | Gln | Lys | Lys | Val<br>335 | Glu  | Asn  | Ala | Ala   | Lys<br>340 | Gln | Ala | Ģlu | Lys  | Arg<br>345              |   |        |     | .* |     |   |
|                   | Ser   | Glu | Glu | Glu | Glu<br>350 | Ala  | Pro  | Pro | Asp   | Gly<br>355 | Ala | Val | Ala | Glu  | Tyr<br>360              |   |        |     |    | •   |   |
| •                 | ,     |     |     | •   | 365        |      |      |     |       | 370        |     |     |     |      | 375                     | • |        |     |    |     |   |
|                   |       |     |     |     | 380        |      | •    |     |       | 385        |     |     |     |      | 390                     |   |        |     |    |     |   |
|                   | Gln   |     |     |     | 395        |      |      |     |       | 400        |     |     |     |      | 405                     | ě |        |     |    | · . | , |
|                   | Asn   | Asp | Ile | Pro | Glu<br>410 |      | Glu  | Val | . Glu | 415        |     | Glu | Gly | Trp  | Met<br>420              |   |        |     |    |     |   |
|                   |       |     |     |     |            |      |      |     |       |            |     |     |     |      |                         |   |        |     |    |     | • |
| ·                 |       |     |     |     |            |      |      |     |       |            |     |     |     |      |                         |   |        |     |    |     |   |
|                   |       |     |     |     |            |      |      |     |       |            |     |     |     |      |                         |   |        |     |    |     |   |

Ser His Val Leu Gln Phe Glu Asp Lys Ser Arg Lys Val Lys Asp 430. Ala Ser Met Gln Asp Ser Asp Thr Phe Glu Ile Tyr Asp Pro Arg 445 . Asn Pro Val Asn Lys Arg Arg Glu Glu Ser Lys Lys Leu Met 455 Arg Glu Lys Lys Glu Arg Arg 470 <210> 246 <211> 24 <212> DNA <213> Artificial Sequence <223> Synthetic oligonucleotide probe <400> 246 tgcggagatc ctactggcac aggg 24 <210> 247 <211> 18 <212> DNA <213> Artificial Sequence <223> Synthetic oligonucleotide probe <400> 247 cgagttagtc agagcatg 18 <210> 248 ' <211> 18 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 248 cagatggtgc tgttgccg 18 <210> 249 <211> 29 <212> DNA <213> Artificial Sequence <223> Synthetic oligonucleotide probe <400> 249 caactggaac aggaactgag atgtggatc 29 <210> 250

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Gly Thr Gly Thr Ser Ser Asn Pro Ser Val Gly Leu Asn Phe Gly 35

Asn Leu Gly Ser Thr Ser Thr Pro Ala Thr Thr Ser Ala Pro Ser 50 55 60

Ser Gly Phe Gly Thr Gly Leu Phe Gly Ser Lys Pro Ala Thr Gly
65 70 75

Phe Thr Leu Gly Gly Thr Asn Thr Gly Ala Leu His Thr Lys Arg

Pro Gln Val Val Thr Lys Tyr Gly Thr Leu Gln Gly Lys Gln Met 95 100 105

His Val Gly Lys Thr Pro Ile Gln Val Phe Leu Gly Val Pro Phe 110 115 120

Ser Arg Pro Pro Leu Gly Ile Leu Arg Phe Ala Pro Pro Glu Pro 125 130 135

| . <del></del> . | Pro | Glu     | Pro   | Trp      | Lys<br>140 | Gly | Ile | Arg | Asp | Ala<br>145  | Thr | Thr | Tyr     | Pro | Pro 150           |     |       |    |      |         |
|-----------------|-----|---------|-------|----------|------------|-----|-----|-----|-----|-------------|-----|-----|---------|-----|-------------------|-----|-------|----|------|---------|
|                 | Gly | Trp     | Ser   | Leu      | Ala<br>155 | Leu | Ser | Pro | Gly | Trp<br>160  |     | Ala | Val     | Ala | Arg<br>165        |     |       |    |      |         |
|                 | Ser | Arg     | Leu   | Thr      | Ala<br>170 | Thr | Ser | Ala | Ser | Arg<br>175  | Val | Gln | Ala     | Ser | Leu<br>180        |     |       |    |      |         |
|                 | Leu | Pro     | Gln   | Pro      | Leu<br>185 | Ser | Val | Trp | Gly | Tyr<br>190  | Arg | Cys | Leu     | Gln | Glu<br>195        |     |       |    |      |         |
|                 | Ser | Trp     | Gly   | Gln      | Leu<br>200 | Ala | Ser | Met | Tyr | Val<br>205  | Ser | Thr | Arg     | Glu | Arg<br>210        |     |       |    |      |         |
|                 | Tyr | Lys<br> | Trp   | Leu<br>- | Arg<br>215 | Phe | Ser | Glu | Asp | Cys<br>.220 | Leu | Tyr | Leu<br> | Asn | Val<br>_225       |     | <br>· |    | <br> | .·<br>- |
|                 |     |         |       |          | 230        |     |     | •   |     | 235         |     |     |         | Val | 240               |     |       |    |      |         |
|                 |     |         |       |          | 245        |     |     |     | •   | 250         |     |     |         | -   | Ser<br>255        | . * |       |    |      |         |
|                 |     |         |       |          | 260        |     |     |     |     | 265         |     |     |         | Leu | 270               |     |       |    |      | ,       |
|                 |     |         |       |          | 275        |     |     |     | • • | 280         |     |     |         | Thr | 285               |     |       |    |      |         |
|                 |     |         |       |          | 290        |     |     |     |     | 295         |     |     |         | Met | 300               |     |       | ٠. | •    | •       |
|                 |     | •       |       |          | 305        |     |     | •   |     | 310         |     |     |         | Gly | 315               |     |       |    |      |         |
|                 |     |         |       |          | 320        |     |     |     |     | 325         |     |     |         |     | Ser<br>330        |     | •     |    |      |         |
|                 |     |         |       |          | 335        |     |     |     |     | 340         |     |     |         | Phe | 345               |     |       | ·  |      |         |
|                 |     | ,       |       |          | 350        |     |     |     |     | 355         |     |     |         |     | Ile<br>360        |     |       |    | •    |         |
|                 |     |         |       |          | 365        |     | •   |     |     | 370         |     | ,   |         |     | Ala<br>375<br>Arg |     |       |    | •    |         |
|                 | 4   |         |       |          | 380        | 1   |     |     |     | 385         |     |     |         |     | 390<br>Arg        |     |       |    |      |         |
|                 |     |         |       |          | 395        | i . |     |     |     | 400         | ) . |     |         |     | 405<br>Trp        |     | •     | •  |      |         |
|                 | ·   | : Let   | . 611 | ı ne     | 410        |     |     |     | ,   | 415         |     |     |         |     | 420               |     |       |    |      |         |
|                 |     |         | •     |          |            |     | ٠   |     |     |             |     |     |         |     |                   |     |       |    | •    |         |
|                 |     |         |       |          |            |     |     |     |     |             |     |     | ٠.      |     |                   |     |       |    |      |         |

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425
Leu Val Leu Leu Thr Gln Gly Lys Val Ser Ser Val Pro Tyr Leu
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Leu Gly Val Asn Asn Leu Glu Phe Asn Trp Leu Leu Pro Tyr Asn
               455
Ile Thr Lys Glu Gln Val Pro Leu Val Val Glu Glu Tyr Leu Asp
                                   475
Asn Val Asn Glu His Asp Trp Lys Met Leu Arg Asn Arg Met Met
                485
Asp Ile Val Gln Asp Ala Thr Phe Val Tyr Ala Thr Leu Gln Thr
  _ ___ _ 500 _ _ _ - 510
Ala His Tyr His Arg Glu Thr Pro Met Met Gly Ile Cys Pro Ala
Gly His Ala Thr Thr Arg Met Lys Ser Thr Cys Ser Trp Ile Leu
Pro Gln Glu Trp Ala
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| ctat                             | ggag       | ta g   | CCat | LCLL       | L Ly |           | LLLA | CLL |            | au c | aauc | cege | 2   | , 50       |
|----------------------------------|------------|--------|------|------------|------|-----------|------|-----|------------|------|------|------|-----|------------|
| tcac                             | ctta       | .aa a  | aaa  | 2764       |      |           | •    |     |            | •    |      | •    |     |            |
| <210><br><211><br><212><br><213> | 544<br>PRT | •<br>• | pien | s          |      |           |      |     |            |      |      |      |     |            |
| <400>                            | 259        | )      |      |            |      |           |      |     |            |      |      |      |     |            |
| Met<br>1                         | Leu        | Leu    | Pro  | Leu<br>5   | Leu  | Leu       | Ser  | Ser | Leu<br>10  | Leu  | Gly  | Gly  | Ser | Gln<br>15  |
| Ala                              | Met        | Asp.   | Ģly  | Arg<br>20  |      | Trp       | Ile  | Arg | Val_<br>25 | Gln_ | Glu_ | Ser  | Val | Met<br>30  |
| Val                              | Pro        | Glu    | Gly  | Leu<br>35  | Cys. | Ile       | Ser  | Val | Pro<br>40  | Cys  | Ser  | Phe  | Ser | Tyr<br>45  |
| Pro                              | Arg        | Gln    | Asp  | Trp<br>50  | Thr  | Gly       | Ser  | Thr | Pro<br>55  | Ala  | Tyr. | Gly  | Tyr | Trp<br>60  |
| Phe                              | Lys        | Ala    | Val  | Thr<br>65  | Glu  | Thr       | Thr  | Lys | Gly<br>70  | Ala  | Pro  | Val  | Ala | Thr<br>75  |
| Asn                              | His        | Gln    | Ser  | Arg<br>80  | Glu  | Val       | Glu  | Met | Ser<br>85  | Thr  | Arg  | Gly  | Arg | Phe<br>90  |
| Gln                              | Leu        | Thr    | Gly  | Asp<br>95  | Pro  | Ala       | Lys  | Gly | Asn<br>100 | Cys  | Ser  | Le'u | Val | Ile<br>105 |
| Arg                              | Asp        | Ala    | Gln  | Met<br>110 |      | Asp       | Glu  | Ser | Gln<br>115 | Tyr  | Phe  | Phe  | Arg | Val<br>120 |
| Glu                              | Arg        | Gly    | Ser  | Tyr<br>125 | Val  | Thr       | Tyr  | Asn | Phe<br>130 | Met  | Asn  | Asp  | Gly | Phe<br>135 |
| Phe                              | Leu        | Lys    | Val  | Thr<br>140 | Val  | Leu<br>·. | Ser  | Phe | Thr<br>145 | Pro  | Arg  | Pro  | Gln | Asp<br>150 |
| His                              | Asn        | Thr    | Asp  | Leu<br>155 | Thr  | Cys       | His  | Val | Asp<br>160 | Phe  | Ser  | Arg  | Lys | Gly<br>165 |
| Val                              | Ser        | Ala    | Gln  | Arg<br>170 | Thr  | Val       | Arg  | Leu | Arg<br>175 | Val  | Ala  | Tyr  | Ala | Pro<br>180 |
| Arg                              | Asp        | Leu    | Val  | Ile<br>185 | Ser  | Ile       | Ser  | Arg | Asp<br>190 |      | Thr  | Pro  | Ala | Leu<br>195 |
| Glu                              | Pro        | Gln    | Pro  | Gln<br>200 | Gly  | Asn       | Val  | Pro | Tyr<br>205 | Leu  | Glu  | Ala  | Gln | Lys<br>210 |
| Gly                              | Gln        | Phe    | Leu  | Arg<br>215 |      | Leu       | Cys  | Ala | Ala<br>220 | Asp  | Ser  | Gln  | Pro | Pro<br>225 |

agaaataacc ataaaagtgg gcaaccagca gctctaggcg ctgctcttgt 2700

|    | Ala | Thr   | Leu   |  |   | Val   | Leu   | Gln  | Asn   | Arg<br>235   | Val  | Leu   | Ser  | Ser  | Ser<br>240   |
|----|-----|---|---|--|---|---|---|--|---|--|--|---|--|--|--|
|    | His | Pro   | Trp   | Gly  | Pro<br>245  | Arg   | Pro   | Leu  | Gly   | Leu<br>250   | Glu  | Leu   | Pro  | Gly  | Val<br>255   |
|    | Lys | Ala   | Gly   | Asp.   | Ser<br>260  | Gly   | Arg   | Tyr  | Thr   | Cys<br>265   | Arg  | Ala   | Glu  | Asn  | Arg<br>270   |
|    | Leu | Gly   | Ser   | Gln  | Gln<br>275  | Arg   | Ala   | Leu  | Asp   | Leu<br>280   | Ser  | Val   | Gln  | Tyr  | Pro<br>285   |
| ٠  | Pro | Glu   | Asn   | Leu  | Arg<br>290  | Val   | Met   | Val  | Ser   | Gln<br>295   | Ala  | Asn   | Arg  | Thr  | Val<br>300   |
|    | Leu | G <u>l</u> u  | Asn   | <u>Leu</u>   | Gly<br>305  | _Asn  | Gly.  | Thr  | Ser_  | Leu<br>310   | _Pro   | Val   | _Leu   | .Glu.  | Gly<br>315   |
|    | Gln | Ser   | Leu   | Cys  | Leu<br>320  | Val   | Cys   | Val  | Thr   | His<br>325   | Ser  | Ser   | Pro  | Pro  | Ala<br>.330  |
|    | Arg | Leu   | Ser   | Trp  | Thr<br>335  | Gln   | Arg   | Gly  | Gln   | Val<br>340   | Leu  | Ser   | Pro  | Ser  | Gln<br>345   |
|    | Pro | Ser   | Asp   | Pro  | Gly<br>350  | Val   | Leu   | Glu  | Leu   | Pro<br>355   | Arg  | Val   | Gln  | Val  | Glu<br>360   |
|    | His | Glu   | Gly   | Glu  | Phe<br>365  | Thr   | Cys   | His  | Ala   | Arg<br>370   | His  | Pro   | Leu  | Gly  | Ser<br>375   |
|    | Gln | His   | Val   | Ser  | Leu<br>380  | Ser   | Leu   | Ser  | Val   | His<br>385   | Tyr  | Lys   | Lys  | Gly  | Leu<br>390   |
| •. | Ile | Ser   | Thr   | Ala  | Phe<br>395  | Ser   | Asn   | Gly  | Ala   |  |  | Gly   | Ile  | Gly  | 11e<br>405   |
| Ť  |     | ٠   |   |  | 410   |   |   |  |   | 415  | -  |   |  |  | 420  |
|    | Leu | Pro   | Lys   | Arg  |   |   | Gln   | Thr  | Glu   | Thr<br>430   | Pro  | Arg   | Pro  | Arg  | Phe<br>435   |
|    |     |   |   |  | 440   |   | •   |  |   | 445  |  |   |  |  | 450  |
|    | Ala | Gly   | Pro   | Leu  |   |   | Lys   | Arg  | Asn   | Gln<br>460   | Lys  | Ala   | Thr  | Pro  | 465  |
|    | Ser | Pro   | Arg   | Thr  |   |   | Pro   | Pro  | Gly   |  |  | Ser   | Pro  | Glu  | Ser<br>480   |
|    | Lys | Lys   | Asn   | Gln  |   |   | Glr   | туг  | Glr   |  |  | Ser   | : Phe  | Pro  | 495  |
| -  | Pro | Lys   | Ser   | Ser  |   |   | a Ala   | Pro  | Glu   |  |  | n Glu   | ı Ser  | Glr  | Glu<br>510   |
|    |     | Lys Leu Pro Leu Gln Arg Pro His Gln Ile Thr Leu Ser Ala Ser | His Pro Lys Ala Leu Gly Pro Glu Leu Glu Gln Ser Arg Leu Pro Ser His Glu Gln His Ile Ser Thr Ala Leu Pro Ser Arg Ala Gly Ser Pro | His Pro Trp  Lys Ala Gly  Leu Gly Ser  Pro Glu Asn  Leu Glu Asn  Gln Ser Leu  Arg Leu Ser  Pro Ser Asp  His Glu Gly  Gln His Val  Ile Ser Thr  Thr Ala Leu  Leu Pro Lys  Ser Arg His  Ala Gly Pro  Ser Pro Arg | His Pro Trp Gly  Lys Ala Gly Asp  Leu Gly Ser Gln  Pro Glu Asn Leu  Leu Glu Asn Leu  Gln Ser Leu Cys  Arg Leu Ser Trp  Pro Ser Asp Pro  His Glu Gly Glu  Gln His Val Ser  Ile Ser Thr Ala  Thr Ala Leu Leu  Leu Pro Lys Arg  Ser Arg His Ser  Ala Gly Pro Leu  Ser Pro Arg Thr  Lys Lys Asn Gln | His Pro Trp Gly Pro 245  Lys Ala Gly Asp Ser 260  Leu Gly Ser Gln Gln 275  Pro Glu Asn Leu Arg 290  Leu Glu Asn Leu Gly 305  Gln Ser Leu Cys Leu 320  Arg Leu Ser Trp Thr 335  Pro Ser Asp Pro Gly 350  His Glu Gly Glu Phe 365  Gln His Val Ser Leu 380  Ile Ser Thr Ala Phe 395  Thr Ala Leu Leu Phe 410  Leu Pro Lys Arg Arg 425  Ser Arg His Ser Thr 440  Ala Gly Pro Leu Ala 455  Ser Pro Arg Thr Pro 470  Lys Lys Asn Gln Lys 485 | His Pro Trp Gly Pro Arg 245  Lys Ala Gly Asp Ser Gly 260  Leu Gly Ser Gln Gln Arg 275  Pro Glu Asn Leu Arg Val 290  Leu Glu Asn Leu Gly Asn 305  Gln Ser Leu Cys Leu Val 320  Arg Leu Ser Trp Thr Gln 335  Pro Ser Asp Pro Gly Val 350  His Glu Gly Glu Phe Thr 365  Gln His Val Ser Leu Ser 380  Ile Ser Thr Ala Phe Ser 395  Thr Ala Leu Leu Phe Leu 410  Leu Pro Lys Arg Arg Thr 425  Ser Arg His Ser Thr Ile 440  Ala Gly Pro Leu Ala Gln 455  Ser Pro Arg Thr Pro Pro 470  Lys Lys Asn Gln Lys Lys 485 | His Pro Trp Gly Pro Arg Pro 245  Lys Ala Gly Asp Ser Gly Arg 260  Leu Gly Ser Gln Gln Arg Ala 275  Pro Glu Asn Leu Arg Val Met 290  Leu Glu Asn Leu Gly Asn Gly 305  Gln Ser Leu Cys Leu Val Cys 320  Arg Leu Ser Trp Thr Gln Arg 335  Pro Ser Asp Pro Gly Val Leu 350  His Glu Gly Glu Phe Thr Cys 365  Gln His Val Ser Leu Ser Leu 380  Ile Ser Thr Ala Phe Ser Asn 395  Thr Ala Leu Leu Phe Leu Cys 410  Leu Pro Lys Arg Arg Thr Gln 425  Ser Arg His Ser Thr Ile Leu 440  Ala Gly Pro Leu Ala Gln Lys 455  Ser Pro Arg Thr Pro Pro 470  Lys Lys Asn Gln Lys Lys Glr 485  Pro Lys Ser Ser Thr Gln Ala | Lys Ala Gly Asp Ser Gly Arg Tyr 260  Leu Gly Ser Gln Gln Arg Ala Leu 275  Pro Glu Asn Leu Arg Val Met Val 290  Leu Glu Asn Leu Gly Asn Gly Thr 305  Gln Ser Leu Cys Leu Val Cys Val 320  Arg Leu Ser Trp Thr Gln Arg Gly 335  Pro Ser Asp Pro Gly Val Leu Glu 350  His Glu Gly Glu Phe Thr Cys His 365  Gln His Val Ser Leu Ser Leu Ser 380  Ile Ser Thr Ala Phe Ser Asn Gly 395  Thr Ala Leu Leu Phe Leu Cys Leu 410  Leu Pro Lys Arg Arg Thr Gln Thr 425  Ser Arg His Ser Thr Ile Leu Asp 440  Ala Gly Pro Leu Ala Gln Lys Arg 455  Ser Pro Arg Thr Pro Pro Pro Pro Pro 470  Lys Lys Asn Gln Lys Lys Gln Tyr 485  Pro Lys Ser Ser Thr Gln Ala Pro | His Pro Trp Gly Pro Arg Pro Leu Gly 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr 260  Leu Gly Ser Gln Gln Arg Ala Leu Asp 275  Pro Glu Asn Leu Arg Val Met Val Ser 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser 305  Gln Ser Leu Cys Leu Val Cys Val Thr 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln 335  Pro Ser Asp Pro Gly Val Leu Glu Leu 350  His Glu Gly Glu Phe Thr Cys His Ala 365  Gln His Val Ser Leu Ser Leu Ser Val 380  Ile Ser Thr Ala Phe Ser Asn Gly Ala 395  Thr Ala Leu Leu Phe Leu Cys Leu Ala 410  Leu Pro Lys Arg Arg Thr Gln Thr Glu 425  Ser Arg His Ser Thr Ile Leu Asp Tyr 440  Ala Gly Pro Leu Ala Gln Lys Arg Asn 455  Ser Pro Arg Thr Pro Pro Pro Pro Gly 470  Lys Lys Asn Gln Lys Lys Gln Tyr Glr 485  Pro Lys Ser Ser Thr Gln Ala Pro Glr | ### Pro Trp Gly Pro Arg Pro Leu Gly Leu 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr Cys 260  Leu Gly Ser Gln Gln Arg Ala Leu Asp Leu 275  Pro Glu Asn Leu Arg Val Met Val Ser Gln 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser Leu 305  Gln Ser Leu Cys Leu Val Cys Val Thr His 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln Val 335  His Glu Gly Glu Phe Thr Cys His Ala Arg 365  Gln His Val Ser Leu Ser Leu Ser Val His 380  The Ser Thr Ala Phe Ser Asn Gly Ala Phe 395  Thr Ala Leu Leu Phe Leu Cys Leu Ala Leu 410  Leu Pro Lys Arg Arg Thr Gln Thr Glu Thr 425  Ser Arg His Ser Thr Ile Leu Asp Tyr Ile 440  Ala Gly Pro Leu Ala Gln Lys Arg Asn Gln Arg Cly Ala 470  Lys Lys Asn Gln Lys Lys Gln Tyr Gln Leu 485  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Thr Gln Ala Pro Glu Ser Crow Arg Thr Pro Pro Pro Pro Gly Ala 470  Lys Lys Ser Ser Thr Gln Ala Pro Glu Ser Arg Cly Ser Ser Arg Cly Arg Cly Arg C | His Pro Trp Gly Pro Arg Pro Leu Gly Leu Glu 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr Cys Arg 265  Leu Gly Ser Gln Gln Arg Ala Leu Asp Leu Ser 275  Pro Glu Asn Leu Arg Val Met Val Ser Gln Ala 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser Leu Pro 305  Gln Ser Leu Cys Leu Val Cys Val Thr His Ser 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln Val Leu 335  His Glu Gly Glu Phe Thr Cys His Ala Arg His 365  Gln His Val Ser Leu Ser Leu Ser Val His Tyr 380  The Ser Thr Ala Phe Ser Asn Gly Ala Phe Leu 410  Thr Ala Leu Leu Phe Leu Cys Leu Ala Leu Ile 410  Ser Arg His Ser Thr Ile Leu Asp Tyr Ile Asr 440  Ala Gly Pro Leu Ala Gln Lys Arg Asn Gln Lys Lys Asn Gln Lys Lys Gln Tyr Gln Leu Pro 475  Lys Lys Asn Gln Lys Lys Gln Tyr Gln Leu Pro 490  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Glr Arg Cys Lys Ser Gln Lys Lys Gln Tyr Gln Leu Pro 490  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Glr Arg Cys Lys Ser Ser Thr Gln Ala Pro Glu Ser Glr Arg Arg Cyp Cys Lys Ser Gln Lys Lys Gln Tyr Gln Leu Pro 485  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Glr Arg Cyp | His Pro Trp Gly Pro Arg Pro Leu Gly Leu Glu Leu 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr Cys Arg Ala 265  Leu Gly Ser Gln Gln Arg Ala Leu Asp Leu Ser Val 280  Pro Glu Asn Leu Arg Val Met Val Ser Gln Ala Asn 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser Leu Pro Val 305  Gln Ser Leu Cys Leu Val Cys Val Thr His Ser Ser 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln Val Leu Ser 335  Pro Ser Asp Pro Gly Val Leu Glu Leu Pro Arg Val 355  His Glu Gly Glu Phe Thr Cys His Ala Arg His Pro 365  Gln His Val Ser Leu Ser Leu Ser Val His Tyr Lys 380  Ile Ser Thr Ala Phe Ser Asn Gly Ala Phe Leu Gly 395  Thr Ala Leu Leu Phe Leu Cys Leu Ala Leu Ile Ile 410  Leu Pro Lys Arg Arg Thr Gln Thr Glu Thr Pro Arg 425  Ser Arg His Ser Thr Ile Leu Asp Tyr Ile Asn Val 440  Ala Gly Pro Leu Ala Gln Lys Arg Asn Gln Lys Ala 460  Pro Lys Asn Gln Lys Lys Gln Tyr Gln Leu Pro Ser 485  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Gln Gl | His Pro Trp Gly Pro Arg Pro Leu Gly Leu Glu Leu Pro 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr Cys Arg Ala Glu 260  Leu Gly Ser Gln Gln Arg Ala Leu Asp Leu Ser Val Gln 275  Pro Glu Asn Leu Arg Val Met Val Ser Gln Ala Asn Arg 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser Leu Pro Val Leu 305  Gln Ser Leu Cys Leu Val Cys Val Thr His Ser Ser Pro 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln Val Leu Ser Pro 335  Pro Ser Asp Pro Gly Val Leu Glu Leu Pro Arg Val Gln 355  His Glu Gly Glu Phe Thr Cys His Ala Arg His Pro Leu 365  Gln His Val Ser Leu Ser Leu Ser Val His Tyr Lys Lys 380  Ile Ser Thr Ala Phe Ser Asn Gly Ala Phe Leu Gly Ile 400  Thr Ala Leu Leu Phe Leu Cys Leu Ala Leu Ile Ile Met 410  Leu Pro Lys Arg Arg Thr Gln Thr Glu Thr Pro Arg Pro 425  Ser Arg His Ser Thr Ile Leu Asp Tyr Ile Asn Val Val 440  Ala Gly Pro Leu Ala Gln Lys Arg Asn Gln Lys Ala Thr 455  Ser Pro Arg Thr Pro Pro Pro Gly Ala Pro Ser Pro 470  Lys Lys Asn Gln Lys Lys Gln Tyr Gln Leu Pro Ser Phe 485  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Gln Glu S | His Pro Trp Gly Pro Arg Pro Leu Gly Leu Glu Leu Pro Gly 245  Lys Ala Gly Asp Ser Gly Arg Tyr Thr Cys Arg Ala Glu Asn 260  Leu Gly Ser Gln Gln Arg Ala Leu Asp Leu Ser Val Gln Tyr 275  Pro Glu Asn Leu Arg Val Met Val Ser Gln Ala Asn Arg Thr 290  Leu Glu Asn Leu Gly Asn Gly Thr Ser Leu Pro Val Leu Glu 305  Gln Ser Leu Cys Leu Val Cys Val Thr His Ser Ser Pro Pro 320  Arg Leu Ser Trp Thr Gln Arg Gly Gln Val Leu Ser Pro Ser 335  Pro Ser Asp Pro Gly Val Leu Glu Leu Pro Arg Val Gln Val 355  His Glu Gly Glu Phe Thr Cys His Ala Arg His Pro Leu Gly 365  Gln His Val Ser Leu Ser Leu Ser Val His Tyr Lys Lys Gly 380  Ile Ser Thr Ala Phe Ser Asn Gly Ala Phe Leu Gly 11e Gly 400  Thr Ala Leu Leu Phe Leu Cys Leu Ala Leu Ile Ile Met Lys 415  Leu Pro Lys Arg Arg Thr Gln Thr Glu Thr Pro Arg Pro Arg 425  Ser Arg His Ser Thr Ile Leu Asp Tyr Ile Asn Val Val Pro 445  Ala Gly Pro Leu Ala Gln Lys Arg Asn Gln Lys Ala Thr Pro 460  Ser Pro Arg Thr Pro Pro Pro Gly Ala Pro Ser Pro Glu 475  Lys Lys Asn Gln Lys Lys Gln Tyr Gln Leu Pro Ser Phe Pro 485  Pro Lys Ser Ser Thr Gln Ala Pro Glu Ser Gln Glu Ser Gln |

Glu Leu His Tyr Ala Thr Leu Asn Phe Pro Gly Val Arg Pro Arg Pro Glu Ala Arg Met Pro Lys Gly Thr Gln Ala Asp Tyr Ala Glu 535 Val Lys Phe Gln <210> 260 <211> 22 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 260 caaagcctgc gcctggtctg tg 22 <210> 261 <211>. 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 261 ttctggagcc cagagggtgc tgag 24 <210> 262 · <211> 45 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 262 ggagctgcca cccattcaaa tggagcacga aggagagttc acctg 45 <210> 263 <211> 2857 <212> DNA <213> Homo sapiens <400> 263 tgaagagtaa tagttggaat caaaagagtc aacgcaatga actgttattt 50 actgctgcgt tttatgttgg gaattcctct cctatggcct tgtcttggag 100 caacagaaaa ctctcaaaca aagaaagtca agcagccagt gcgatctcat 150 ttgagagtga agcgtggctg ggtgtggaac caatttttg taccagagga 200

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<sup>&</sup>lt;210> 264

<sup>&</sup>lt;211> 772

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 264

| •   |    |          |     |       |     |            |     |     |       |       |            |     |            |     |        |            |      |      |     |   |
|-----|----|----------|-----|-------|-----|------------|-----|-----|-------|-------|------------|-----|------------|-----|--------|------------|------|------|-----|---|
|     |    |          |     |       | ,   |            |     |     |       |       |            |     |            |     |        |            |      |      |     |   |
|     |    |          |     |       |     |            |     |     |       |       |            |     |            |     |        |            |      |      |     |   |
|     |    | Met<br>1 | Asn | Cys   | Tyr | Leu<br>5   | Leu | Leu | Arg   | Phe   | Met<br>10. | Leu | Gly        | Ile | Pro    | Leu<br>15  | •    |      |     |   |
| . • |    | Leu      | Trp | Pro   | Cys | Leu<br>20  | Gly | Ala | Thr   | Glu   | Asn<br>25  | Ser | Gln        | Thr | Lys    | Lys<br>30  |      |      |     |   |
| •   |    | Val      | Lys | Gln   | Pro | Val<br>35  | Arg | Ser | His   | Leu   | Arg<br>40  | Val | Lys        | Arg | Gly    | Trp<br>45  |      |      |     |   |
|     |    | Val      | Trp | Asn   | Gln | Phe        | Phé | Val | Pro   | Glu   | Glu        | Met | Asn        | Thr | Thr    | Ser        |      |      |     |   |
|     |    | His      | His | Ile   | Gly | 50<br>Gln  | Leu | Arg | Ser   | Asp   | 55<br>Leu  | Asp | Asn        | Gly | Asn    | 60<br>Asn  |      |      | . • |   |
|     |    |          |     |       |     | 65<br>Lys  |     | :   |       |       | 70         |     |            |     |        | 75         |      |      |     | * |
|     |    | <br>     |     |       |     | 80         |     |     |       |       | 85         |     | _ <u> </u> |     |        | . 90       | :    | <br> |     |   |
|     |    | Ile      | Ile | Asp   | Glu | Arg<br>95  | Thr | Gly | Asp   | Ile   | Tyr<br>100 | Ala | Ile        | Gln | Lys    | Leu<br>105 |      |      |     |   |
|     |    | Asp      | Arg | Ģlu   | Glu | Arg<br>110 | Ser | Leu | Tyr   | Ile   | Leu<br>115 | Arg | Ala        | Gln | Val    | Ile<br>120 |      |      |     |   |
|     |    | Asp      | Ile | Ala   |     | Gly<br>125 | Arg | Ala | Val   | Glu   | Pro<br>130 | Glu | Ser        | Glu | Phe    | Val        |      |      | •   |   |
|     | ٠. | Ile      | Lys | Val   |     |            | Ile | Asn | Asp   | Asn   | .Glu       |     | Lys        | Phe | Leu    | Asp<br>150 |      |      |     |   |
|     |    | Glu      | Pro | Tyr   | Glu | Ala        | Ile | Val | Pro   | Glu   | Met        | Ser | Pro        | Glu | Gly    | Thr        |      |      |     |   |
|     |    | Leu      | Val | Ile   | Gln | 155<br>Val | Thr | Ala | Ser   | Asp   |            | Asp | Asp        | Pro | Ser    | 165<br>Ser |      | . •  |     |   |
|     |    | Glv      | Asn | Asn   | Ala | 170<br>Ara | Leu | Leu | Tvr   | Ser   | 175<br>Leu |     | Gln        | Gly | Gln    | 180<br>Pro |      |      |     |   |
|     |    |          |     |       |     | 185        |     |     |       |       | 190        |     |            | •   |        | 195<br>Ser |      |      |     |   |
|     |    |          |     |       |     | 200        |     |     |       |       | 205        | :   | ٠.         |     |        | 210        |      |      |     |   |
| e . |    | Lys      | Met | . Asp | Arg | Glu<br>215 |     | Gln | . Asp | Glu   | 220        |     | vai        | 11e | : lite | 225        |      |      |     |   |
|     |    | Ala      | Lys | Asp   | Met | Ile<br>230 |     | Gln | Pro   | o Gly | Ala<br>235 |     | Ser        | Gly | Thr    | Thr<br>240 |      |      |     |   |
|     |    | Ser      | Val | Leu   | Ile | Lys<br>245 |     | Ser | Asp   | Val   | Asn<br>250 |     | Asn        | Lys | Pro    | 255        |      |      |     |   |
|     |    | Phe      | Lys | Glu   | Ser | Leu<br>260 |     | Arg | g Leu | 1 Thr | Val<br>265 |     | Glu        | Ser | Ala    | Pro<br>270 |      |      |     | * |
|     |    | Thr      | Gl? | / Thr | Ser | 1le<br>275 |     | Thr | Ile   | e Met | : Ala      |     | Asp        | Asr | n Asp  | 285        |      | •    |     |   |
|     |    |          |     |       |     |            |     |     |       |       |            |     |            |     |        |            |      |      |     |   |
|     |    |          |     |       |     |            |     |     |       |       |            |     |            |     |        | ,          |      |      |     |   |
| •   |    |          |     |       |     |            |     |     |       |       |            |     |            |     |        |            | ., 1 |      |     |   |
|     |    |          |     |       |     |            |     |     |       |       |            |     |            | -   |        | *          |      |      |     |   |

| •   |     |       |     |     |              |     |     |     |     |            |     |      |       |     |               |
|-----|-----|-------|-----|-----|--------------|-----|-----|-----|-----|------------|-----|------|-------|-----|---------------|
|     |     |       |     |     |              |     |     |     |     |            |     |      |       |     |               |
|     | Gly | Glu   | Asn | Ala | Glu<br>290   | Met | Asp | Tyr | Ser | Ile<br>295 | Glu | Glu  | Asp   | Asp | Ser<br>300    |
|     | Gln | Thr   | Phe | Asp | Ile<br>305   | Ile | Thr | Asn | His | Glu<br>310 | Thr | Gln  | Glu   | Gly | Ile<br>315    |
|     | Val | Ile   | Leu | Lys | Lys<br>320   | Lys | Val | Asp | Phe | Glu<br>325 | His | Gln  | Asn   | His | Tyr<br>330    |
|     | Gly | Ile   | Arg | Ala | Lys<br>335   | Val | Lys | Asn | His | His<br>340 | Val | Pro  | Glu   | Gln | Leu<br>345    |
|     | Met | Lys   | Tyr | His | Thr<br>350   | Glu | Ala | Ser | Thr | Thr<br>355 | Phe | Ile  | Lys   | Ile | Gln<br>360    |
|     | Val | Glu   | Asp | Val | Asp<br>365   | Glu | Pro | Pro |     | Phe<br>370 |     | Leu  | Pro   | Tyr | Tyr<br>_375 . |
|     | Val | Phe   | Glu | Val | Phe<br>380   | Glu | Glu | Thr | Pro | Gln<br>385 | Gly | Ser  | Phe   | Val | Gly<br>390    |
|     | Val | Val   | Ser | Ala | Thr<br>395   | Asp | Pro | Asp | Asn | Arg<br>400 | Lys | Ser  | Pro   | Ile | Arg<br>405    |
|     | Tyr | Ser   | Ile | Thr | Arg<br>410   | Ser | Lys | Val | Phe | Asn<br>415 | Ile | Asn  | Asp   | Asn | Gly<br>420    |
|     | Thr | Ile   | Thr | Thr | Ser<br>425   | Asn | Ser | Leu | Asp | Arg<br>430 | Glu | Ile  | Ser   | Ala | Trp<br>435    |
|     | Tyr | Asn   | Leu | Ser | Ile<br>440   | Thr | Ala | Thr | Glu | Lys<br>445 | Tyr | Asn  | Ile   | Glu | Gln<br>450    |
|     | Ile | Ser   | Ser | Ile | Pro<br>455   | Leu | Tyr | Val | Gln | Val<br>460 | Leu | Asn  | Ile   | Asn | Asp<br>465    |
| * . | His | Ala   | Pro | Glu | Phe<br>470   |     | Gln | Tyr | Tyr | Glu<br>475 |     | Tyr  | Val   | Cys | Glu<br>480    |
|     | Asn | Ala   | Gly | Ser | Gly<br>485   |     | Val | Ile | Gln | Thr<br>490 |     | Ser  | Ala   | Val | Asp<br>495    |
|     | Arg | Asp   | Glu | Ser | Ile<br>500   |     | Glu | His | His | Phe<br>505 |     | Phe  | Asn   | Leu | Ser<br>510    |
|     | Val | Glu   | Asp | Thr | Asn<br>515   |     | Ser | Ser | Phe | Thr<br>520 |     | Ile  | Asp   | Asn | Gln<br>525    |
|     | Asp | Asn   | Thr | Ala | . Val<br>530 |     | Leu | Thr | Asn | Arg<br>535 |     | Gly  | Phe   | Asn | Leu<br>540    |
|     | Gln | Glu   | Glu | Pro | Val<br>545   |     | Tyr | Ile | Ser | 550        |     | ılle | Ala   | Asp | Asn<br>555    |
|     | Gly | / Ile | Pro | Ser | Leu<br>560   |     | Ser | Thr | Asn | Thr<br>565 |     | Thr  | : Ile | His | Val<br>570    |
|     |     |       |     |     |              |     |     |     |     |            |     |      |       |     |               |
|     |     |       |     |     |              |     |     |     |     |            |     |      |       |     |               |
|     |     |       |     |     |              | ٠   |     |     |     |            |     |      |       |     |               |

|   | Cys<br>'     | Asp     | Cys   | Gly    | Asp<br>575 | Ser   | Gly   | Ser  | Thr   | Gln<br>580 | Thr   | Cys   | Gln  | Tyr  | Gln<br>585        |  |
|---|--------------|---------|-------|--------|------------|-------|-------|------|-------|------------|-------|-------|------|------|-------------------|--|
|   | Glu          | Leu     | Val   | Leu    | Ser<br>590 | Met   | Gly   | Phe  | Lys   | Thr<br>595 | Glu   | Val   | Ile  | Ile  | Ala<br>600        |  |
|   | Ile          | Leu     | Ile   | Cys    | Ile<br>605 | Met   | Ile   | Ile  | Phe   | Gly<br>610 | Phe   | Ile   | Phe  | Leu  | Thr<br>615        |  |
|   | Leu          | Ģly     | Leu   | Lys    | Gln<br>620 | Arg   | Arg   | Lys  | Gln   | Ile<br>625 | Leu   | Phe   | Pro  | Glu  | <b>Lys</b><br>630 |  |
|   | Ser          | Glu     | Asp   | Phe    | Arg<br>635 |       | Asn   | Ile  | Phe   | Gln<br>640 | Tyr   | Asp   | Asp  | Glu  | Gly<br>645        |  |
| _ | Gly          | Gly<br> | Glu   | Glu    | Asp<br>650 | Thr   | Glu   | Ala  | Phe   | Asp<br>655 | Ile   | Ala   | Glu  | Leu  | Arg<br>. 660.     |  |
|   | Ser          | Ser     | Thr   | Ile    | Met<br>665 | Arg   | Glu   | Arg  | Lys   | Thr<br>670 | Arg   | Lys   | Thr  | Thr  | Ser<br>675        |  |
|   | Ala          | Glu     | Ile   | Arg    | Ser<br>680 | Leu   | Tyr   | Arg  | Gln   | Ser<br>685 | Leu   | Gln   | Val  | Gly  | Pro<br>690        |  |
|   | Asp          | Ser     | Ala   | Ile    | Phe<br>695 | Arg   | Lys   | Phe  | Ile   | Leu<br>700 | Glu   | Lys   | Leu  | Glu  | Glu<br>705        |  |
|   | Ala          | Asn     | Thr   | Asp    | Pro<br>710 | Cys   | Ala   | Pro  |       | Phe<br>715 | Asp   | Ser   | Leu  | Gln  | Thr<br>720        |  |
|   | Tyr          | Ala     | Phe   | Glu    | Gly<br>725 |       | Gly   | Ser  | Leu   | Ala<br>730 |       | Ser   | Leu  | Ser  | Ser<br>735        |  |
|   | Leu          | Glu     | Ser   | Àla    | Val<br>740 |       | Asp   | Gln  | Asp   | Glu<br>745 |       | Tyr   | Asp  | Tyr  | Leu<br>750        |  |
|   | Asn          | Glu     | Leu   | Gly    | Pro<br>755 |       | , Phe | Lys  | Arg   | Leu<br>760 |       | Cys   | Met  | Phe  | Gly<br>765        |  |
|   | Ser          | Ala     | . Val | Gln    | Ser<br>770 |       | Asn   | 1    |       |            |       |       |      | ÷    | , •               |  |
|   | <210         | > 26    | 5     |        |            |       |       |      |       |            |       |       |      |      |                   |  |
|   | <211         |         |       |        |            |       |       |      |       |            |       |       |      |      |                   |  |
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|   |              |         |       | -,     |            |       |       |      |       |            |       |       | •    |      |                   |  |
|   | <220<br><221 |         | sure  | •      |            |       |       |      |       | •          |       |       |      |      |                   |  |
|   | <222         |         |       |        |            | 26,   | 228,  | 249  | , 25  | 52         |       |       |      |      |                   |  |
|   | <223         | ∕ un    | KHOV  | vii Dā | 156        |       |       |      |       | •          |       |       |      |      |                   |  |
|   | <400<br>att  |         |       | cago   | cata       | itt t | ttnt  | gtt  | ga ad | ccaa       | caaca | a gga | gtca | ataa | 50                |  |
|   | gaa          | tatt    | ttn   | taaa   | aatgo      | gat a | agaga | acto | gc aa | agat       | gagta | a ttg | ggta | aatc | 100               |  |

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Leu Gly Trp Ile Gly Ala Ile Val Ser Thr Ala Leu Pro Gln Trp

<sup>&</sup>lt;210> 270

<sup>&</sup>lt;211> 211

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 270

Met Ala Asn Ala Gly Leu Gln Leu Leu Gly Phe Ile Leu Ala Phe
1 10 15

| Arg  | Ile  | Tyr | Ser | Tyr<br>35  | Ala | Gly | Asp | Asn | Ile<br>40  | Val | Thr | Ala | Gln | Ala<br>45   |
|------|------|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|-------------|
| Met  | Tyr  | Glu | Gly | Leu<br>50  | Trp | Met | Ser | Cys | Val<br>55  | Ser | Gln | Ser | Thr | Gly<br>60   |
| Gln  | Ile  | Gln | Cys | Lys<br>65  | Val | Phe | Asp | Ser | Leu<br>70  | Leu | Asn | Leu | Ser | Ser<br>75   |
| Thr  | Leu  | Gln | Ala | Thr<br>80  | Arg | Ala | Leu | Met | Val<br>85  | Val | Gly | Ile | Leu | Leu<br>90   |
| Gly  | Val  | Ile | Ala | Ile<br>95  | Phe | Val | Ala | Thr | Val        |     | Met | Lys | Cys | Met<br>105  |
| Lys  | Cys  | Leu | Glu | Asp<br>110 | Asp | Glu | Val | Gln | Lys<br>115 | Met | Arg | Met | Ala | Val<br>120  |
| Ile  | Gly  | Gly | Ala | Ile<br>125 | Phe | Leu | Leu | Ala | Gly<br>130 | Leu | Ala | Ile | Leu | Val<br>135  |
| Ala  | Thr  | Åla | Trp | Tyr<br>140 | Gly | Asn | Arg | Ile | Val<br>145 |     | Glu | Phe | Tyr | Asp<br>150  |
| Pro  | Met  | Thr | Pro | Val<br>155 | Asn | Ala | Arg | Tyr | Glu<br>160 | Phe | Gly | Gln | Ala | Leu<br>165  |
| Phe  | Thr  | Gly | Trp | Ala<br>170 | Ala | Ala | Ser | Leu | Cys<br>175 |     | Leu | Gly | Gly | Ala<br>180  |
| Leu  | Leu  | Cys | Cys | Ser<br>185 | Cys | Pro | Arg | Lys | Thr<br>190 |     | Ser | Tyr | Pro | Thr.<br>195 |
| Pro  | Arg  | Pro | Tyr | Pro<br>200 | Lys | Pro | Ala | Pro | Ser<br>205 |     | Gly | Lys | Asp | Tyr<br>210  |
| Val  |      |     |     |            |     |     |     |     |            |     |     |     |     | . ·         |
| -210 | . 27 | 1   |     |            |     |     |     |     |            |     |     |     |     |             |

<210> 271

<211> 564

<212> DNA

<213> Homo sapiens

<220>

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<222> 21, 69, 163, 434, 436, 444

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<400> 271

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ctgtggatgt ccngcgtgtc gcagagcacc gggcagatcc agtgcaaagt 200 ctttgactcc ttgctgaatc tgagcagcac attgcaagca acccgtgcct 250 tgatggtggt tggcatcetc ctgggagtga tagcaatctt tgtggccacc 300 gttggcatga agtgtatgaa gtgcttggaa gacgatgagg tgcagaagat 350 gaggatggct gtcattgggg gcgcgatatt tcttcttgca ggtctggcta 400 ttttagttgc cacagcatgg tatggcaata gaancnttca acanttctat 450 gaccctatga ccccagtcaa tgccaggtac gaatttggtc aggctctctt 500 cactggctgg gctgctgctt ctcttgcct tctgggaggt gccctacttt 550

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<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> 30, 49, 102, 141, 147, 171, 324-325, 339-341

<223> unknown base

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acategtgae egeeeaggee ntgtacgagg ggetgtggat gteetgegtg 200
tegeagagea eegggeagat eeagtgeaaa gtetttgaet eeettgetga 250
atetgageag cacattgeaa geaaceegtg eettgatggt ggttggeate 300
eteetgggag tgatageaat ettnntggee acegttgtnn ntgaagtgta 350
tgaagtgett ggaagaegat gaggtgeaga agatgaggat ggetgteatt 400
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<212> DNA

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<220>

<221> unsure

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cattgggggc gcgatattc ttcttgcagg tctggctatt tnnngttgcc 400
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cccagtcaat gccaggtacg aatttggtca ggctctctc actggctggg 500
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<210> 274

<211> 526

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> 25, 50, 60, 123, 127, 370, 395, 397-398, 402-403, 405-407

<223> unknown base

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ceagtgeaaa gtetttgact eettgetgaa tetgageage acattgeaag 200

caaceegtge ettgatgggg ttggeateet eetgggagtg atageaacet 250

ttgtggeeae eggtggeatg aagtgtatga agtgettgga agaegatgag 300

gtgeeagaag atgaggatgg etgteattgg gggegegata tttettgttg 350

caggtetgge tatttagtn geeacageat ggtatggeaa tagantnntt 400

enngnnntet atgaeeetat gaeeeeagte aatgeeaggt aegaatttgg 450

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<210> 275
<211> 398
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> 22, 61, 91, 144, 238-239, 262, 265-266, 271, 274
<223> unknown base
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<211> 495
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> 39, 58, 130, 234, 314, 364, 427, 450, 461, 476
<223> unknown base
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 tgcttggaag acgatgaggt gcagaagatg aggatggctg tcattggggg 300
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<210> 277
<211> 200
<212> DNA .
<213> Homo sapiens
<220>
<221> unsure
<222> 34, 87, 138, 147, 163, 165-166, 172
<223> unknown base
<400>. 277
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<210> 278
<211> 542
<212> DNA
<213> Homo sapiens
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<221> unsure
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<223> unknown base
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<213> Homo sapiens
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<221> unsure
<222> 90, 115, 147, 228, 387
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<210> 279

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<211> 2285
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<213> Homo sapiens
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Met Ala Lys Val Glu Gln Val Leu Ser Leu Glu Pro Gln His Glu

<sup>&</sup>lt;210> 284

<sup>&</sup>lt;211> 243

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 284

| , 1   | L .               |                  |       |             | 5 .   |     | ٠,  |       | 10           | )       |       |       |       | 15          |
|-------|-------------------|------------------|-------|-------------|-------|-----|-----|-------|--------------|---------|-------|-------|-------|-------------|
| Leu   | ı Ly              | s Ph             | e Ar  | g Gl        | y Pro | Phe | th: | Asp   | o Val<br>25  | Val     | . Thi | r Thi | : Asr | Leu<br>30   |
| Lys   | Le                | u Gl             | y As  | n Pro       | Thi   | Asp | Arc | J Asr | Val          | Cys     | Ph∈   | e Lys | Val   | L Lys<br>45 |
|       |                   |                  |       | 30          | ,     |     |     |       | 55           |         |       |       |       | / Ile<br>60 |
|       |                   |                  |       | y Ala<br>65 | ,     | . 4 |     |       | 70           |         | •     |       |       | 75          |
|       |                   |                  |       | Pro<br>80   |       |     |     |       | 85           | , . · · |       |       |       | 90          |
|       |                   |                  |       | e-Ala<br>95 |       |     |     |       | · 100        | ٠. ٠.   |       |       | •     | 105         |
| Trp   | Lys               | Glu              | ı Ala | 110         | Pro   | Glu | Asp | Leu   | Met<br>115   | Asp     | Ser   | Lys   |       | Arg         |
| Cys   | Val               | Phe              | e Glu | Leu<br>125  | Pro   | Ala | Glu | Asn   | Asp<br>130   | Lys     | Pro   | His   | Asp   | Val<br>135  |
| Glu   | Ile               | Asn              | Lys   | Ile<br>140  | Ile   | Ser | Thr | Thr   | Ala<br>145   | Ser     | Lys   | Thr   | Glu   | Thr<br>150  |
| Pro   | Ile               | V <sub>a</sub> l | Ser   | Lys<br>155  | Ser   | Leu | Ser | Ser   | Ser<br>160   | Leu     | Asp   | Asp   | Thr   | Glu<br>165  |
| Val   | Lys               | Lys              | Val   | Met<br>170  | Glu   | Glu | Cys | Lys   | Arg<br>175   | Leu     | Gln   | Gly   | Glu   | Val<br>180  |
| Gln   | Arg               | Leu              | Arg   | Glu<br>185  | Glu   | Asn | Lys | Gln   | Phe 190      | Lys     | Glu   | Glu   | Asp   | Gly<br>195  |
| Leu . | Arg               | Met              | Aŗg   | Lys<br>200  | Thr   | Val | Gln | Ser   | Asn<br>205   | Ser     | Pro   | Ile   |       | Ala<br>210  |
| Leu   | Ala               | Pro              | Thr   | Gly<br>215  | Lys   | Glu | Glu | Gly   | Leu<br>220   | Ser !   | Thr   | Arg   |       | Leu<br>225  |
| Ala 1 | Leu               | Val              | Val   | Leu<br>230  | Phe   | Phe | Ile | Val ( | Gly '<br>235 | Val 1   | lle   | Ile ( |       | Lys<br>240  |
| Ile A | Al <sub>.</sub> a | Leu              |       |             |       | :   | ,   |       |              |         |       |       |       |             |
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<210> 285 <211> 418 <212> DNA <213> Homo sapiens

<220>

<221> unsure

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cagcagtttt gggtggggag caagggnnga gagaaactct tcagcgaatc 200

cttctagtac tagttgagag tttgactgtg aattaatttt atgccataaa 250

agacnaaccc agttctgttt gactatgtag catcttgaaa agaaaaatta 300

taataaagcc ccaaaattaa gaattctttt gtcattttgt cacatttgct 350

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gttaacttta aaatgagc 418

<210> 286

<211> 543

<212> DNA

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<221> unsure

<222> 73, 97

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gtcccaegt ggcccaetee eggeceagge tgettteegt gtetteagtt 200
ctgtccaage cateagetee ttgggaetga tgaacagagt cagaageea 250
aaggaattge cactgtggea geateagaeg taetegteat aagtgagagg 300
egtgtgttga etgattgace eagegettg gaaataaatg geagtgett 350
gttcaettaa agggaecaag etaaattgta ttggtteatg tagtgaagte 400
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<210> 287

<211> 270

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<221> unsure
<222> 38, 64, 72, 164, 198, 200, 220, 222, 229, 242
<223> unknown base
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 catatccatg ggatttaaat ttatcataac catgtgtaaa aagaaattaa 150
 tgtatgatga catntcacag gtattgcctt taaattaccc atccctgnan 200
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 agttaaaaat gtatagtaac 270
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<211> 428
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
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<223> unknown base
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 gccatcagct ccttgggact gatgaacaga gtcagaagcc caaaggaatt 100
 gcactgtggc agcatnagac gtacttgtna taagtgagag gcgtgtgttg 150
 actgattgac ccagcgcttt ggaaataaat ggcagtgctt tgttcantta 200
 aagggaccaa gctaaatttg tattggttca tgtagtgaag tcaaactgtt 250
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 tgttttctta ttgtcacaag agtacagtta atgctgcgtg ctgctgaant 350
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gaaataaatg gcagtgcttt gttcacttaa agggaccaag ctaaatttgt 200
attggttcat gtagtgaagt caaactgtta ttcagagatg tttaatgcat 250
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<211> 609

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> 57, 60, 186, 235, 244, 304, 339, 355, 359, 361, 387, 432, 441, 447, 481, 513, 532, 584, 598

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 aaccaccaga gccaagagcc ggg 23
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Thr Leu Ile Asp Gly Ser Glu Met Glu Trp Asp Phe Met Trp His

<sup>&</sup>lt;210> 296

<sup>&</sup>lt;211> 413

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 296

Met Glu Asn Met Leu Leu Trp Leu Ile Phe Phe Thr Pro Gly Trp  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

|     | ,          |     |     | 20         |     |     |     |       | 25         |     |       |     |     | 30         |
|-----|------------|-----|-----|------------|-----|-----|-----|-------|------------|-----|-------|-----|-----|------------|
| Leu | Arg        | Lys | Val | Pro<br>35  | Arg | Ile | Val | Ser   | Glu<br>40  | Arg | Thr   | Phe | His | Leu<br>45  |
| Thr | Ser        | Pro | Ala | Phe<br>50  | Glu | Ala | Asp | Ala   | Lys<br>55  | Met | Met   | Val | Asn | Thr<br>60  |
| Val | Cys        | ďlу | Île | Glu<br>65  | Cys | Gln | Lys | Glu   | Leu<br>70  | Pro | Thr   | Pro | Ser | Leu<br>75  |
| Ser | Glu        | Leu | Glu | Asp<br>80  | Tyr | Leu | Ser | Tyr   | Glu<br>85  | Thr | Val   | Phe | Glu | Asn<br>90  |
| Gly | Thr        | Arg | Thr | Leu<br>95  | Thr | Arg | Val | Lys   | Val<br>100 |     | Asp   | Leu | Val | Leu<br>105 |
| Glu | Pro        | Thr | Gln | Asn<br>110 | Ile | Thr | Thr | Lys   | Gly<br>115 | Val | Ser   | Val | Arg | Arg<br>120 |
| Lys | Arg        | Gln | Val | Tyr<br>125 | Gly | Thr | Asp | Ser   | Arg<br>130 | Phe | Ser   | Ile | Leu | Asp<br>135 |
| Lys | Arg        | Phe | Leu | Thr<br>140 | Asn | Phe | Pro | Phe   | Ser<br>145 | Thr | Ala   | Val | Lys | Leu<br>150 |
| Ser | Thr        | Gly | Cys | Ser<br>155 | Gly | Ile | Leu | Ile   | Ser<br>160 |     | Gln   | His | Val | Leu<br>165 |
| Thr | Ala        | Ala | His | Cys<br>170 | Val | His | Asp | Gly   | Lys<br>175 |     | Tyr   | Val | Lys | Gly<br>180 |
| Ser | Lys        | Lys | Leu | Arg<br>185 | Val | Gly | Leu | Leu   | Lys<br>190 |     | Arg   | Asn | Lys | Ser<br>195 |
| Gly | Gly        | Lys | Lys | Arg<br>200 |     | Gly | Ser | Lys   | Arg<br>205 |     | Arg   | Arg | Glu | Ala<br>210 |
| Ser | Gly<br>, · | Gly | Asp | Gln<br>215 |     | Glu | Gly | Thr   | Arg<br>220 |     | His   | Leu | Gln | Glu<br>225 |
| Arg | Ala        | Lys | Gly | Gly<br>230 | Arg | Arg | Arg | Lys   | Lys<br>235 | Ser | Gly   | Arg | Gly | Gln<br>240 |
| Arg | Ile        | Ala | Glu | Gly<br>245 |     | Pro | Ser | Phe   | 250        |     | Thr   | Arg | Val | Lys<br>255 |
| Asn | Thr        | His | Ile | Pro<br>260 |     | Gly | Trp | Ala   | Arg<br>265 |     | Gly   | Met | Gly | 270        |
| Ala | Thr        | Leu | Asp | Tyr<br>275 |     | Tyr | Ala | Let   | 280        |     | ı Lev | Lys | Arg | Ala<br>285 |
| His | Lys        | Lys | Lys | Tyr        |     | Glu | Leu | ı Gly | / Ile      | Ser | Pro   | Thr | Ile | Lys        |

Lys Met Pro Gly Gly Met Ile His Phe Ser Gly Phe Asp Asn Asp

Arg Ala Asp Gln Leu Val Tyr Arg Phe Cys Ser Val Ser Asp Glu . 320 325 330

Ser Asn Asp Leu Leu Tyr Gln Tyr Cys Asp Ala Glu Ser Gly Ser 335 340 345

Thr Gly Ser Gly Val Tyr Leu Arg Leu Lys Asp Pro Asp Lys Lys 350 355 360

Asn Trp Lys Arg Lys Ile Ile Ala Val Tyr Ser Gly His Gln Trp 365 370 375

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<210> 301 <211> 525 <212> PRT <213> Homo sapiens

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115

| Pro | Lys   | Val   | Leu   | Asp<br>140  | Gly | Thr | Arg   | Cys   | <br>Tyr<br>145. | Thr        | Glu   | Ser   | Leu | Asp<br>150   |
|-----|-------|-------|-------|-------------|-----|-----|-------|-------|-----------------|------------|-------|-------|-----|--------------|
| Met | Cys   | Ile   | Ser   | Gly<br>155  | Leu | Cys | Gln   | Ile   | Val<br>160      | Gly        | Cys   | Asp   | His | Gln<br>165   |
| Leu | Gly   | Ser   | Thr   | Val<br>170  | Lys | Ģlu | Asp   | Asn   | Cys<br>175      | Gly        | Val   | Cys   | Asn | Gly<br>180   |
| Asp | Gly   | Ser   | Thr   | Cys<br>185  | Arg | Leu | Val   | Arģ   | Gly<br>190      | Gln        | Tyr   | Lys   | Ser | Gln .<br>195 |
| Leu | Ser   | Ala   | Thr   | Lys<br>200  | Ser | Asp | Asp   | Thr   | Val<br>205      | Val        | Ala   | Leu   | Pro | Tyr<br>210   |
| Gly | Ser   | Arg   | His   | Ile<br>215_ | Arg | Leu | Val   | Leu   | Lys<br>220      | Gly        | Pro   | Asp   | His | Leu<br>225   |
| Tyr | Leu   | Gļlu  | Thr   | Lys<br>230  | Thr | Leu | Gln   | Gly   | Thr<br>235      | Lys        | Gly   | Glu   | Asn | Ser<br>240   |
| Leu | Ser   | Ser   | Thr   | Gly<br>245  | Thr | Phe | Leu   | Val   | Asp<br>250      | Asn        | Ser   | Ser   | Val | Asp<br>255   |
| Phe | Gln   | Lys   | Phe   | Pro<br>260  | Asp | Lys | Glu   | Ile   | Leu<br>265      | Arg        | Met   | Ala   | Gly | Pro<br>270   |
| Leu | Thr   | Ala   | Asp   | Phe<br>275  | Ile | Val | Lys   | Ile   | Arg<br>280      |            | Ser   | Gly   | Ser | Ala<br>285   |
| Asp | Ser   | Thr   | Val   | Gln<br>290  | Phe | Ile | Phe   | Tyr   | Gln<br>295      |            | Ile   | Ile   | His | Arg<br>300   |
| Trp | Arg   | Glu   | Thr   | Asp<br>305  | Phe | Phe | Pro   | Cys   | Ser<br>310      | Ala        | Thr   | Cys   | Gly | Gly<br>315   |
| Gly | Tyr   | Gln   | Leu   | Thr<br>320  |     | Ala | Glu   | Cys   | Tyr<br>325      | Asp        | Leu   | Arg   | Ser | Asn<br>330   |
| Arg | Val   | Val   | Ala   | Asp<br>335  | Gln | Tyr | Cys   | His   | Tyr<br>340      |            | Pro   | Glu   | Asn | Ile<br>345   |
| Lys | Pro   | Lys   | Pro   | Lys<br>350  |     | Gln | Glu   | Cys   | 355             |            | Asp   | Pro   | Cys | Pro<br>360   |
| Ala | Ser   | Asp   | Gly   | Tyr<br>365  |     | Gln | Ile   | . Met | 370             |            | Asp   | Leu   | Tyr | His<br>375   |
| Pro | Leu   | Pro   | Arg   | Trp<br>380  |     | Ala | Thr   | Pro   | 385             |            | Ala   | Cys   | Ser | Ser<br>390   |
| Sei | Cys   | Gly   | 7 Gly | Gly<br>395  |     | Gln | Ser   | Arg   | Ala<br>400      |            | l Ser | Cys   | Val | Glu<br>405   |
| Gli | ı Asp | o Ile | e Gln | Gly<br>410  |     | Val | . Thi | Sei   | 415             | l Glu<br>5 | ı Glu | ı Trp | Lys | 420          |

 Met
 Tyr
 Thr
 Pro
 Lys
 Met
 Pro
 Ile
 Ala
 Gln
 Pro
 Cys
 Asn
 Ile
 Phe

 Asp
 Cys
 Pro
 Lys
 Trp
 Leu
 Ala
 Gln
 Glu
 Trp
 Ser
 Pro
 Cys
 Thr
 Val

 Thr
 Cys
 Gly
 Leu
 Arg
 Tyr
 Arg
 Val
 Val
 Leu
 Cys
 Ile
 Asp

 His
 Arg
 Gly
 Met
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 Thr
 Gly
 Gly
 Cys
 Ser
 Pro
 Lys
 Thr
 Lys
 Pro

 His
 Ile
 Lys
 Glu
 Cys
 Ile
 Val
 Pro
 Thr
 Pro
 Cys
 Tyr
 Lys
 Pro

 Lys
 Glu
 Lys
 Leu
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 Val
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 Ala
 Lys
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<210> 302

<211> 1533

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Val Leu Ile Thr Gly Ala Asn Ser Gly Leu Gly Arg Ala Thr Ala 50 55 60

Ala Glu Leu Leu Arg Leu Gly Ala Arg Val Ile Met Gly Cys Arg
65 70 75

Asp Arg Ala Arg Ala Glu Glu Ala Ala Gly Gln Leu Arg Arg Glu 80 85 90

Leu Arg Gln Ala Ala Glu Cys Gly Pro Glu Pro Gly Val Ser Gly

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| Ser          | Val  | Arg       | Ala | Phe<br>125 | Cys | Gln | Glu | Met | Leu<br>130 | Gln     | Glu | Glu: | Pro | Arg<br>135 |
| Leu          | Asp  | Val       | Leu | Ile<br>140 | Asn | Asn | Ala | Gly | Ile<br>145 | Phe     | Gln | Cys  | Pro | Tyr<br>150 |
| Met          | Lys  | Thr       | Glu | Asp<br>155 | Gly | Phe | Glu | Met | Gln<br>160 | Phe     | Gly | Val  | Asn | His<br>165 |
| Leu          | Gly  | His       | Phe | Leu<br>170 | Leu | Thr | Asn | Leu |            | Leu<br> | -   |      | Leu | Lys<br>180 |
| Ser          | Ser  | Ala       | Pro | Ser<br>185 | Arg | Ile | Val | Val | Val<br>190 | Ser     |     | Lys  | Leu | Tyr<br>195 |
| Lys          | Tyr  | Gly       | Asp | Ile<br>200 | Asn | Phe | Asp | Asp | Leu<br>205 | Asn     | Ser | Glu  | Gln | Ser<br>210 |
| Tyr          | Asn  | Lys       | Ser | Phe<br>215 | Cys | Tyr | Ser | Arg | Ser<br>220 | Lys     | Leu | Ala  | Asn | Ile<br>225 |
| Leu          | ·Phe | Thr       | Arg | Glu<br>230 | Leu | Ala | Arg | Arg | Leu<br>235 | Glu     | Gly | Thr  | Asn | Val<br>240 |
| Thr          | Val  | Asn       | Val | Leu<br>245 | His | Pro | Gly | Ile | Val<br>250 |         | Thr | Asn  | Leu | Gly<br>255 |
| Arg          | His  | Ile       | His | Ile<br>260 | Pro | Leu | Leu | Val | Lys<br>265 |         | Leu | Phe  | Asn | Leu<br>270 |
| Val          | Ser  | Trp       | Ala | Phe<br>275 |     | Lys | Thr | Pro | Val<br>280 |         | Gly | Ala  | Gln | Thr<br>285 |
| Ser          | Ile  | Tyr<br>·. | Leu | Ala<br>290 | Ser | Ser | Pro | Glu | Val<br>295 |         | Gly | Val  | Ser | Gly<br>300 |
| Arg          | Tyr  | Phe       | Gly | Asp<br>305 |     | Lys | Glu | Glu | Glu<br>310 |         | Leu | Pro  | Lys | Ala<br>315 |
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190

185

| Gly                  | Asp  | Val | Ser | Lys<br>200 | Pro | Glu | Arg         | Tyr | Ser<br>205 | Gly          | Asp | Asn  | Ile | Ile<br>210  |
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| Tyr                  | Lys  | Pro | Pro | Gly<br>215 | His | Ser | Ala         | Pro | Asp<br>220 | Met          | Val | Tyr  | Leu | Gly<br>225  |
| Ala                  | Met  | Thr | Asn | Phe<br>230 | Asp | Val | Thr         | Tyr | Asn<br>235 | Trp          | Ile | Gln  | Asp | Lys<br>240  |
| Cys                  | Val  | Pro | Leu | Val<br>245 | Arg | Glu | Ile         | Thr | Phe<br>250 | Glu          | Asn | Gly  |     | Glu<br>255  |
| Leu                  | Thr  | Glu | Glu | Gly<br>260 | Leu | Pro | Phe         | Leu | Ile<br>265 | Leu          | Phe | His  | Met | Lys<br>270  |
| Glu                  | Asp  | Thr | Glu | Ser<br>275 | Leu | Glu | <u>I</u> le | Phe | Gln<br>280 | Asn          | Glu | _Val | Ala | Arg.<br>285 |
| Gln                  | Leu  | Ile | Ser | Glu<br>290 | Lys | Gly | Thr         | Ile | Asn<br>295 | Phe          | Leu | His  | Ala | Asp<br>300  |
| Cys<br>              | Asp  | Lys | Phe | Arg<br>305 | His | Pro | Leu         | Leu | His<br>310 | Ile          | Gln | Lys  | Thr | Pro<br>315  |
| Ala                  | Asp  | Cys | Pro | Val<br>320 | Ile | Ala | Ile         | Asp | Ser<br>325 | Phe          | Arg | His  | Met | Tyr<br>330  |
| Val                  | Phe  | Gly | Asp | Phe<br>335 | Lys | Asp | .Val        | Leu | Ile<br>340 | Pro          | Gly | Lys  | Leu | Lys<br>345  |
| Gln                  | Phe  | Val | Phe | Asp<br>350 | Leu | His | Ser         | Gly | Lys<br>355 | Leu          | His | Arg  | Glu | Phe<br>360  |
| His                  | His  | Gly | Pro | Asp<br>365 | Pro | Thr | Asp         | Thr | Ala<br>370 | Pro          | Gly | Glu  | Gln | Ala<br>375  |
| Gln                  | Asp  | Val | Ala | Ser<br>380 | Ser | Pro | Pro         | Glu | Ser<br>385 | Ser          | Phe | Gln  | Lys | Leu<br>390  |
| Åla                  | Pro  | Ser | Glu | Tyr<br>395 |     | Tyr | Thr         | Leu | Leu<br>400 |              | Asp | Arg  | Asp | Glu<br>405  |
| Leu                  |      |     |     |            |     |     |             |     |            | <i>i</i> · . |     |      |     |             |
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<222> 36, 48

<223> unknown base

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Asn Thr Leu Asn Pro Leu Val Leu Pro Glu Tyr Leu Ile His Ala 50 55 60

Phe Phe Cys Val Met Phe Leu Cys Ala Ala Glu Trp Leu Thr Leu 65 70 75

Gly Leu Asn Met Pro Leu Leu Ala Tyr His Ile Trp Arg Tyr Met 80 85 90

Ser Arg Pro Val Met Ser Gly Pro Gly Leu Tyr Asp Pro Thr Thr 95 100 105

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<213> Homo sapiens

<400> 330

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Gly Thr Ala Ser Ala Glu Ala Phe Asp Ser Val Leu Gly Asp Thr

Ala Ser Cys His Arg Ala Cys Gln Leu Thr Tyr Pro Leu His Thr
50 55 60

Tyr Pro Lys Glu Glu Glu Leu Tyr Ala Cys Gln Arg Gly Cys Arg
65 70 75

Leu Phe Ser Ile Cys Gln Phe Val Asp Asp Gly Ile Asp Leu Asn 80 85 90

Arg Thr Lys Leu Glu Cys Glu Ser Ala Cys Thr Glu Ala Tyr Ser 95 100 105

| Gln | Ser              | Asp      | Glu  | Gln<br>110 | Tyr | Ala | Cys         | His   | Leu-<br>115 | Gly | Cys | Gln | Asn   | Gln<br>120 |
|-----|------------------|----------|------|------------|-----|-----|-------------|-------|-------------|-----|-----|-----|-------|------------|
| Leu | Pro              | Phe      | Ala  | Glu<br>125 | Leu | Arg | Gln         | Glu   | Gln<br>130  | Leu | Met | Ser | Leu   | Met<br>135 |
| Pro | Lys              | Met      | His  | Leu<br>140 | Leu | Phe | Pro         | Leu   | Thr<br>145  | Leu | Val | Arg | Ser   | Phe<br>150 |
| Trp | Ser              | Asp      | Met  | Met<br>155 | Asp | Ser | Ala         | Gln   | Ser<br>160  | Phe | Ile | Thr | Ser   | Ser<br>165 |
| Trp | Thr              | Phe      | Tyr  | Leu<br>170 | Gln | Ala | Asp         | Asp   | Gly<br>175  | Lys | Ile | Val | Ile   | Phe<br>180 |
| Gln | Ser              | ŗ'nŝ     | Pro  | Glu<br>185 | Ile | Gln | Ty <u>r</u> | ,Ala, | Pro<br>190  | His | Leu | Glu | Gln   | Glu<br>195 |
| Pro | Thṛ              | Asn      | Leu  | Arg<br>200 | Glu | Ser | Ser         | Leu   | Ser<br>205  | Lys | Met | Ser | Tyr   | Leu<br>210 |
| Gln | Met              | Arg      | Asn  | Ser<br>215 | Gln | Ala | His         | Arg   | Asn<br>220  | Phe | Leu | Glu | Asp   | Gly<br>225 |
| Glu | Ser              | Asp      | Gly  | Phe<br>230 | Leu | Arg | Cys         | Leu   | Ser<br>235  | Leu | Asn | Ser | Gly   | Trp<br>240 |
| Ile | Leu              | Thr      | Thr  | Thr<br>245 |     | Val | Leu         | Ser   | Val<br>250  | Met | Val | Leu | Leu   | Trp<br>255 |
| Ile | Cys              | Cys      | Ala  | Thr<br>260 | Val | Ala | Thr         | Ala   | Val<br>265  | Glu | Gln | Tyr | Val   | Pro<br>270 |
| Ser | <sup>'</sup> Glu | Lys      | Leu  | Ser<br>275 | Ile | Tyr | Gly         | Asp   | Leu<br>280  | Glu | Phe | Met | . Asn | Glu<br>285 |
| Gln | Lys              | Leu      | Asn  | Arg<br>290 | Tyr | Pro | Ala         | Ser   | Ser<br>295  | Leu | Val | Val | Val   | Arg<br>300 |
| Ser | Lys              | Thr      | Glu  | Asp<br>305 |     | Glu | Glu         | Ala   | Gly<br>310  |     | Leu | Pro | Thr   | Lys<br>315 |
| Val | Asn              | Leu      | Ala  | His<br>320 |     | Glu | lle         | •     |             |     |     |     | •     |            |
|     | > 35<br>> DN     | 0 .<br>A | apie | ns         |     |     |             |       |             |     |     |     |       |            |
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<sup>&</sup>lt;211> 468

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 337

Met Gly Arg Gly Trp Gly Phe Leu Phe Gly Leu Leu Gly Ala Val 1 5 10

Trp Leu Leu Ser Ser Gly His Gly Glu Glu Gln Pro Pro Glu Thr 20 25 30

|         | Ala  | Ala | Gln   | Arg    |       | Phe   | Cys | Gln  | Val  |       | Gly | Tyr | Leu   | Asp |         |     |          |     |     |     |     |
|---------|------|-----|-------|--------|-------|-------|-----|------|------|-------|-----|-----|-------|-----|---------|-----|----------|-----|-----|-----|-----|
|         |      |     |       |        | 35    |       |     |      |      | 40.   |     |     |       |     | 45      |     |          |     |     |     |     |
|         | Cys  | Thr | Cys   | Asp    | Val   | Glu   | Thr | Ile  | Asp  | Arg   | Phe | Asn | Asn   | Tyr |         |     |          |     |     |     |     |
|         |      |     |       |        | 50    |       |     |      |      | 55    |     |     |       |     | 60      |     |          |     |     | •   |     |
|         | Leu  | Phe | Pro   | Arg    | Leu   | Gln   | Lys | Leu  | Leu  | Glu   | Ser | Asp | Tyr   | Phe | Arg     |     |          |     |     |     |     |
|         |      |     |       |        | 65    |       |     |      |      | 70    |     |     |       |     | 75      |     |          |     |     |     |     |
|         | Tyr  | Tyr | Lys   | Val    | Asn   | Leu   | Lys | Arg  | Pro  | Cys   | Pro | Phe | Trp   | Asn | Asp     | ,   |          |     |     |     |     |
|         |      |     |       |        | 80    |       |     |      |      | 85    |     |     |       |     | 90      |     |          |     |     |     | •   |
|         | Ile  | Ser | Gln   | Cys    | Gly   | Arg   | Arg | Asp  | Cys  | Ala   | Val | Lys | Pro   | Cys |         |     |          |     |     |     |     |
|         |      |     |       |        | 95    |       |     |      |      | 100   |     |     |       | •   | 105     |     |          |     | ٠.  |     |     |
|         | Ser  | Asp | Glu   | Val    | Pro   | Asp   | Gly | Ile  | Lys  | Ser   | Ala | Ser | Tyr   | Lys | Tyr     |     |          | •   |     |     |     |
|         |      |     |       |        | 110   | -·    |     |      |      | _115  |     |     |       |     | .12.0 _ |     | <br>- :- |     |     | 1   |     |
|         | Ser  | Glu | Glu   | Ala    | Asn   | Asn   | Leu | Ile  | Glu  | Glu   | Cys | Glu | Gln   | Ala | Glu     | •   |          |     |     |     |     |
|         |      |     |       |        | 125   | •     |     |      | •    | 130   |     |     |       |     | 135     |     |          |     |     |     |     |
|         | Arg  | Leu | Gly   | Ala    | Val   | Asp   | Glu | Ser  | Leu  | Ser   | Glu | Glu | Thr   | Gln |         |     |          |     |     |     | :   |
|         |      |     |       |        | 140   |       |     |      |      | 145   |     |     |       |     | 150     |     |          |     |     |     | *,  |
|         | Ala  | Val | Leu   | Gln    | Trp   | Thr   | Lys | His  | Asp. | Asp   | Ser | Ser | Asp   | Asn |         |     |          |     |     |     |     |
|         |      |     |       |        | 155   |       |     |      |      | 160   |     |     |       |     | 165     |     |          |     |     |     |     |
|         | Cys  | Glu | Ala   | Asp    | Asp   | Ile   | Gln | Ser  | Pro  | Glu   | Ala | Glu | Tyr   | Val | Asp     |     |          |     |     |     | • • |
| •       |      |     |       |        | 170   |       |     |      |      | 175   |     |     |       |     | 180     |     |          |     |     |     |     |
| ,       | Leu  | Leu | Leu   | Aşn    | Pro   | Glu   | Arg | Tyr  | Thr  | Gly   | Tyr | Lys | Gly   | Pro | Asp     | •   |          |     |     |     | *   |
| ;<br>vi |      |     |       |        | 185   |       |     |      |      | 190   |     |     |       |     | 195     | ,   | ٠        |     |     |     |     |
|         | Ala  | Trp | Lys   | Ile    | Trp   | Asn   | Val | Ile  | Tyr  | Glu   | Glu | Asn | Cys   | Phe | Lys     |     |          |     |     | • • |     |
|         |      |     |       | ٠.     | 200   |       | : ' |      |      | 205   |     |     |       |     | 210     |     |          |     |     |     |     |
|         | Pro  | Gln | Thr   | Ile    | Lys   | Arg   | Pro | Leu  | Asn  | Pro   | Leu | Ala | Ser   | Gly | Gln     | · : |          |     |     |     |     |
| •       |      |     |       |        | 215   |       |     |      |      | 220   |     |     |       |     | 225     |     |          |     |     |     |     |
|         | Gly  | Thr | Ser   | Glu    | Glu   | Asn   | Thr | Phe  | Tyr  | Ser   | Trp | Leu | Glu   | Gly | Leu     |     |          |     |     |     |     |
|         |      |     |       |        | 230   |       |     |      | , -  | 235   |     |     |       |     | 240     |     |          |     |     |     |     |
|         | Cvs  | Val | . Gĺu | Lvs    | Ara   | Ala   | Phe | Tyr  | Arq  | Leu   | Ile | Ser | Gly   | Leu | His     |     |          | · ; |     |     |     |
| •       | •    |     |       |        | 245   |       |     | -    |      | 250   |     |     |       |     | 255     |     |          |     |     |     |     |
|         | Ala  | Ser | · Ile | . Asn  | ı Val | His   | Leu | Ser  | Ala  | Arq   | Tyr | Leu | Leu   | Gln | Glu     | •   |          |     |     |     |     |
| •       |      | •   |       |        | 260   |       |     |      |      | 265   |     |     |       |     | 270     |     |          |     |     |     |     |
|         | Thr  | Tro | Let   | . Glu  | Lvs   | Lvs   | Trp | Glv  | His  | Asn   | Ile | Thr | Glu   | Phe | Gln     |     |          |     |     |     |     |
|         |      |     |       |        | 275   |       | 1   | 2    | •    | 280   |     |     |       |     | 285     |     | ·        |     |     |     |     |
|         | Gln  | Arc | r Phe | . Asc  | Glv   | , Ile | Leu | Thr  | Glu  | Glv   | Glu | Glv | Pro   | Arg | Arg     |     |          | •   |     |     |     |
|         | 02   |     |       |        |       | )     |     |      |      | 295   |     |     |       |     | . 300   | •   | ;        |     |     |     |     |
|         | T.eu | Lve | . Asr | ı I.e. | ı Tvr | Phe   | Len | īvr  | Leu  | ı Ile | Glu | Leu | . Ard | Ála | Leu     |     |          |     |     |     |     |
|         | 100  | -,- |       |        | 305   |       |     | - 1- |      | 310   |     |     |       |     | 315     |     |          |     |     |     |     |
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|         |      |     |       |        |       |       |     |      |      | •     |     |     |       |     |         |     |          |     | . • |     |     |
| •       |      |     |       |        |       |       |     |      |      |       |     |     |       |     |         |     |          |     |     |     |     |
|         |      |     |       |        |       |       |     |      |      |       |     |     |       |     |         |     |          |     |     |     | _   |

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| Thr | Gly | Asn | Lys | Ile<br>335 | Gln | Asp | Glu | Glu | Asn<br>340 | Lys | Met | Leu | Leu | Leu<br>345 |
| Glu | Ile | Leu | His | Glu<br>350 | Ile | Lys | Ser | Phe | Pro<br>355 | Leu | His | Phe | Asp | Glu<br>360 |
| Asn | Ser | Phe | Phe | Ala<br>365 | Gly | Asp | Lys | Lys | Glu<br>370 | Ala | His | Lys | Leu | Lys 375    |
| Glu | Asp | Phe | Arg | Leu<br>380 | His | Phe | Arg | Asn | Ile<br>385 | Ser | Arg | Ile | Met | Asp<br>390 |
|     |     |     |     |            |     |     |     |     |            |     |     |     | Gln |            |
| Gln | Gly | Leu | Gly | Thr<br>410 | Ala | Leu | Lys | Ile | Leu<br>415 | Phe | Ser | Glu | Lys | Leu<br>420 |
| Ile | Ala | Asn | Met | Pro<br>425 |     | Ser | Gly | Pro | Ser<br>430 | Tyr | Glu | Phe | His | Leu<br>435 |
| Thr | Arg | Gln | Glu | Ile<br>440 | Val | Ser | Leu | Phe | Asn<br>445 | Ala | Phe | Gly | Arg | Ile<br>450 |
| Ser | Thr | Ser | Val | Lys<br>455 | Glu | Leu | Glu | Asn | Phe<br>460 |     | Asn | Leu | Leu | Gln<br>465 |

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<213> Homo sapiens

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65 70 75

Cys Pro Val Gly Gly Ala His Asn Ala Pro Cys Ala Lys Gly His 80 85 90

Leu Gly Asp Tyr Gln Leu Gly Asn Ser Ser His Pro Ala Val Asn 95 100 105

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<211> 311

<212> PRT

<213> Homo sapiens

<400> 352

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Phe Met Trp Phe Phe Tyr Ala Leu Ile Pro Cys Leu Leu Thr Asp

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|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-------|-------------------------|---|---|-----|-----|---|---|--|
|     | Thr | Asn | Met | Lys | His<br>50  | Leu | Leu | Met | Trp | Ser<br>55  |     | Val | Ile | Ala   | Pro<br>60               |   |   |     |     |   |   |  |
|     | Gly | Glu | Thr | Val | Tyr<br>65  | Tyr | Ser | Val | Glu | Tyr<br>70  | Gln | Gly | Glu | Tyr   | Glu<br>75               |   |   |     |     |   | · |  |
|     | Ser | Leu | Tyr | Thr | Ser<br>80  | His | Ile | Trp | Ile | Pro<br>85  | Ser | Ser | Trp | Cys   | Ser<br>90               |   |   |     |     |   |   |  |
|     | Leu | Thr | Glu | Gly | Pro<br>95  | Glu | Cys | Asp | Val | Thr<br>100 | Asp | Asp | Ile | Thr   | Ala<br>105              |   |   |     |     |   |   |  |
|     | Thr | Val | Pro | Tyr | Asn<br>110 |     | Arg |     |     |            | Thr |     |     |       |                         |   |   | · * | · = |   |   |  |
| , . | Thr | Ser | Ala | Trp | Ser<br>125 | Ile | Leu | Lys | His | Pro<br>130 | Phe | Asn | Arg | Asn   | Ser<br>135              |   | • |     |     |   |   |  |
|     | Thr | Ile | Leu | Thr | Arg<br>140 |     | Gly | Met | Glu | Ile<br>145 | Thr | Lys | Asp |       | Phe<br>.150             | · |   |     |     |   |   |  |
| •   | His | Leu | Val | Ile | Glu<br>155 | Leu | Glu | Asp | Leu | Gly<br>160 | Pro | Gln | Phe | Glu   | Phe<br>165              | · |   |     |     |   | , |  |
|     | Leu | Val | Ala | Tyr | Trp<br>170 | Arg | Arg | Glu | Pro | Gly<br>175 | Ala | Glu | Glu | His   | Val <sup>.</sup><br>180 |   |   |     |     | • |   |  |
|     | Lys | Met | Val | Arg | Ser<br>185 | Gly | Gly | Ile | Pro | Val<br>190 |     | Leu | Glu | Thr   | Met<br>195              |   |   |     | ,   |   |   |  |
|     | Glu | Pro | Gly | Ala | Ala<br>200 | Tyr | Cys | Val | Lys | Ala<br>205 |     | Thr | Phe | Val   | Lys<br>210              |   |   |     |     |   |   |  |
|     | Ala | Ile | Gly | Arg |            | Ser | Ala | Phe | Ser | Gln<br>220 |     | Glu | Cys | Val   | Glu<br>225              |   |   |     |     |   |   |  |
|     | Val | Gln | Gly | Glu | Ala<br>230 |     | Pro | Leu | Val | Leu<br>235 |     | Leu | Phe | Ala   | Phe<br>240              |   |   |     |     |   |   |  |
|     | Val | Gly | Phe | Met | Leu<br>245 |     | Leu | Val | Val | Val<br>250 |     | Leu | Phe | Val   | Trp<br>255              |   | , | t   |     |   |   |  |
|     | Lys | Met | Gly | Arg | Leu<br>260 |     | Gln | Tyr | Ser | Cys<br>265 |     | Pro | Val | Val   | Val<br>270              |   |   |     |     |   |   |  |
| . · | Leu | Pro | Asp | Thr | Leu<br>275 |     | Ile | Thr | Asn | Ser<br>280 |     | Gln | Lys | Leu   | 11e<br>285              |   |   |     |     |   |   |  |
|     | Ser | Cys | Arg | Arg | Glu<br>290 |     | Val | Asp | Ala | Cys<br>295 |     | Thr | Ala | . Val | Met<br>300              |   |   |     |     |   |   |  |
|     | Ser | Pro | Glu | Glu | Leu<br>305 |     | Arg | Ala | Trp | 310        |     |     |     |       |                         |   |   |     |     |   |   |  |

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<223> unknown base
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Pro Glu Asp Trp Trp Ser Tyr Lys Asp Asn Leu Gln Gly Asn Phe

Val Pro Gly Pro Pro Phe Trp Gly Leu Val Asn Ala Ala Trp Ser
50 55 60

<sup>&</sup>lt;211> 328

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

| Leu  | Cys | Ala | Val | Gly<br>65  | Lys | Arg | Gln | Ser | Pro.<br>70 | Val | Asp | Val     | Glu | Leu<br>75  |
|------|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|---------|-----|------------|
| Lys  | Arg | Val | Leu | Tyr<br>80  | Asp | Pro | Phe | Leu | Pro<br>85  | Pro | Leu | Arg<br> | Leu | Ser<br>90  |
| Thr  | Gly | Gly | Glu | Lys<br>95  | Leu | Arg | Gly | Thr | Leu<br>100 | Tyr | Asn | Thr     | Gly | Arg<br>105 |
| His  | Val | Ser | Phe | Leu<br>110 | Pro | Ala | Pro | Arg | Pro<br>115 | Val | Val | Asn     | Val | Ser<br>120 |
| Gly  | Gly | Pro | Leu | Leu<br>125 | Tyr | Ser | His | Arg | Leu<br>130 | Ser | Glu | Leu     | Arg | Leu<br>135 |
| Leu  | Phe | Gly | Ala | Arg<br>140 | Asp | Gly | Ala | Gly | Ser<br>145 | Glu | His | Gln     | Ile | Asn<br>150 |
| His. | Gln | Gly | Phe | Ser<br>155 | Ala | Glu | Val | Gln | Leu<br>160 | Ile | His | Phe     | Asn | Gln<br>165 |
| Glu  | Leu | Tyr | Gly | Asn<br>170 | Phe | Ser | Ala | Ala | Ser<br>175 | Arg | Gly | Pro     | Asn | Gly<br>180 |
| Leu  | Ala | Ile | Leu | Ser<br>185 | Leu | Phe | Val | Asn | Val<br>190 | Ala | Ser | Thr     | Ser | Asn<br>195 |
| Pro  | Phe | Leu | Ser | Arg<br>200 | Leu | Leu | Asn | Arg | Asp<br>205 | Thr | Ile | Thr     | Arg | Ile<br>210 |
| Ser  | Tyr | Lys | Asn | Asp<br>215 | Ala | Tyr | Phe | Leu | Gln<br>220 | Asp | Leu | Ser     | Leu | Glu<br>225 |
| Leu  | Leu | Phe | Pro | Glu<br>230 | Ser | Phe | Gly | Phe | Ile<br>235 | Thr | Tyr | Gln     | Gľy | Ser<br>240 |
| Leu  | Ser | Thr | Pro | Pro<br>245 | Cys | Ser | Glu | Thr | Val<br>250 | Thr | Trp | Ile     | Leu | Ile<br>255 |
| Asp  | Arg | Ala | Leu | Asn<br>260 |     | Thr | Ser | Leu | Gln<br>265 | Met | His | Ser     | Leu | Arg<br>270 |
| Leu  | Leu | Ser | Gln | Asn<br>275 |     | Pro | Ser | Gln | Ile<br>280 | Phe | Gln | Ser     | Leu | Ser<br>285 |
| Gly  | Asn | Ser | Arg | Pro<br>290 |     | Gln | Pro | Leu | Ala<br>295 | His | Arg | Ala     | Leu | Arg<br>300 |
| Gly  | Asn | Arg | Asp | Pro<br>305 |     | His | Pro | Glu | Arg<br>310 | Arg | Cys | Arg     | Gly | Pro<br>315 |
| Asn  | Туг | Arg | Leu | His<br>320 |     | Asp | Gly | Val | Pro<br>325 | His | Gly | Arg     | ſ   |            |

<210> 359 <211> 24

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Phe Met Ala Arg Ala Ile Pro Ala Met Val Val Pro Asn Ala Thr 20 25 30

<sup>&</sup>lt;210> 363

<sup>&</sup>lt;211> 500

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 363

Met Lys Cys Thr Ala Arg Glu Trp Leu Arg Val Thr Thr Val Leu
1 5 10 15

| •  |   | Leu | Leu | Glu | Lys | Leu<br>35  | Leu | Glu | Lys | Tyr              | Met<br>40  |     | Glu   | Asp | Gly | Glu<br>45   |
|----|---|-----|-----|-----|-----|------------|-----|-----|-----|------------------|------------|-----|-------|-----|-----|-------------|
|    |   | Trp | Trp | Ile | Ala | Lys<br>50  | Gln | Arg | Gly | Lys              | Arg<br>55  | Ala | Ile   | Thr | Asp | Asn<br>60   |
|    | • | Asp | Met | Gln | Ser | Ile<br>65  | Leu | Asp | Leu | His              | Asn<br>70  | Lys | Leu   | Arg | Ser | Gln<br>75   |
| -  |   | Val | Tyr | Pro | Thr | Ala<br>80  | Ser | Asn | Met | Glu <sub>.</sub> | Tyr<br>85  | Met | Thr   | Trp | Asp | Val<br>90   |
|    |   | Glu | Leu | Glu | Arg | Ser<br>95  | Ala | Glu | Ser | Trp              | Ala<br>100 | Glu | Ser   | Cys | Leu | Trp<br>105  |
|    |   | Glu | His | Gly | Pro | Ala<br>110 | Ser | Leu | Leu | Pro              | Ser<br>115 | Ile | Gly   | Gln | Asn | Leu<br>_120 |
|    |   | Gly | Ala | His | Trp | Gly<br>125 | Arg | Tyr | Arg | Pro              | Pro<br>130 | Thr | Phe   | His | Val | Gln<br>135  |
| ٠. |   | Ser | Trp | Tyr | Asp | Glu<br>140 | Val | Lys | Asp | Phe              | Ser<br>145 |     | Pro   | Tyr | Gļu | His<br>150  |
| 9  |   | Glu | Cys | Asn | Pro | Tyr<br>155 | Cys | Pro | Phe | Arg              | Cys<br>160 | Ser | Gly   | Pro | Val | Cys<br>165  |
| 8  |   | Thr | His | Tyr | Thr | Gln<br>170 | Val | Val | Trp | Ala              | Thr<br>175 | Ser | Asn   | Arg | Ile | Gly<br>180  |
|    |   | Cys | Ala | Ile | Asn | Leu<br>185 | Cys | His | Asn | Met              | Asn<br>190 | Ile | Trp   | Gly | Gln | Ile<br>195  |
|    |   | Trp | Pro | Lys | Ala | Val<br>200 | Tyr | Leu | Val | Cys              | Asn<br>205 | Tyr | Ser   | Pro | Lys | Gly<br>210  |
|    |   | Asn | Trp | Trp | Gly | His<br>215 |     | Pro | Tyr | Lys              | His<br>220 | Gly | Arg   | Pro | Cys | Ser<br>225  |
|    |   | Ala | Cys | Pro | Pro | Ser<br>230 |     | Gly | Gly | Gly              | Cys<br>235 |     | Glu   | Asn | Leu | Cys<br>240  |
|    |   | Tyr | Lys | Glu | Gly | Ser<br>245 |     | Arg | Tyr | Tyr              | Pro<br>250 |     | Arg   | Glu | Glu | Glu<br>255  |
|    |   | Thr | Asn | Glu | Ile | Glu<br>260 |     | Gln | Gln | Ser              | Gln<br>265 |     | His   | Asp | Thr | His<br>270  |
|    |   | Val | Arg | Thr | Arg | Ser<br>275 |     | Asp | Ser | Ser              | Arg<br>280 |     | Glu   | val | Ile | Ser<br>285  |
|    | : | Ala | Glm | Gln | Met | Ser<br>290 |     | Ile | Val | . Ser            | Cys<br>295 |     | ı Val | Arg | Leu | Arg<br>300  |
|    |   | Asp | Gln | Ċys | Lys | Gly<br>305 |     | Thr | Суз | Asr              | Arg        |     | Glu   | Cys | Pro | Ala<br>315  |

| • . |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|-----|---------|-------|-------|-------|----------|-------|------|--------|------------|-------|----------|------|-------|-------|---|---|---|---|----|---|-----|
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   | • |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         | _     | _     | _     | _        |       |      | ** - 1 | <b>-</b> 1 | 01    | C        | 17-1 | 11: - | m     |   |   |   | • |    | • |     |
|     | Gly Cys | Leu   | Asp   |       | Lys      | Ala   | rys  | vaı    |            |       | Ser      | vai  | птѕ   |       |   |   |   |   |    |   |     |
|     |         |       |       | 320   |          |       |      |        | 325        | •     |          |      |       | 330   |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | Glu Met | Gln   | Ser   | Ser   | Ile      | Cys   | Arg  | Ala    | Ala        | Ile   | His      | Tyr  | Gly   | Ile   |   |   |   |   |    |   |     |
|     |         |       |       | 335   |          |       |      |        | 340        |       |          |      |       | 345   |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          | ; -  |       |       |   |   |   |   |    | • |     |
|     | Ile Asp | Asn   | Asp   | Glv   | Glv      | Trp   | Val  | Asp    | Ile        | Thr   | Arg      | Gln  | Gly   | Arq   |   |   |   |   |    |   |     |
|     | 110     |       | ···op | 350   | 1        |       |      |        | 355        |       |          |      | -     | 360   |   |   |   |   |    |   |     |
|     |         |       |       | 330   |          |       |      |        | 555        |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         | -     | 201   | - 1 - | <b>.</b> |       |      | 7      | 7          | C1    | т1.      | Cln  | Th.~  | т10   |   |   |   |   |    |   |     |
|     | Lys His | Tyr   | Pne   |       | Lys      | ser   | Asn  | Arg    |            | Gry   | 116      | GIII | 1111  | 116   |   |   |   |   |    |   |     |
|     |         |       |       | 365   |          |       |      |        | 370        |       |          |      |       | 375   |   |   |   |   |    |   |     |
| •   | •       |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | Gly Lys | Tyr   | Gln   | Ser   | Ala      | Asn   | Ser  | Phe    | Thr        | Val   | Ser      | Lys  | Val   |       |   |   |   |   | •  |   |     |
|     |         |       |       | 380   |          |       | •    |        | 385        |       |          |      |       | 390   |   |   |   |   |    |   |     |
|     | •       |       |       |       |          |       |      |        |            |       |          |      |       | 7     |   |   |   |   |    |   |     |
|     | Val Gln | Ala   | Val   | Thr   | Cvs      | Glu   | Thr  | Thr    | Val        | Glu   | Gln      | Leu  | Cys   | Pro   |   |   |   |   |    |   |     |
|     |         |       |       | 395   | 1000     |       |      |        | 400        | ٠,    |          |      |       | 405   |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       | , · · |   |   |   |   |    |   |     |
| ·   | Dha IIi |       | Dwa   | 71.   | C ~ ~    | u: c  | C    | Pro    | 7 ~~       | Val   | Tur      | Cve  | Pro   | Ara   |   |   |   |   |    |   |     |
|     | Phe His | г гуз | Pro   |       | ser      | пта   | Cys  | PLO    |            | vai   | ıyı      | Cys  | 110   | 420   |   |   |   |   |    | · |     |
| •   |         |       |       | 410   |          |       |      |        | 415        |       |          |      |       | 420   |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       | <b>-</b> |      | 1     |       |   |   |   |   |    |   |     |
|     | Asn Cys | Met   | Gln   | Ala   | Asn      | Pro   | His  | Tyr    |            |       | Val      | lle  | GLY   |       |   |   |   |   |    |   |     |
|     |         |       |       | 425   |          |       |      |        | 430        |       |          |      |       | 435   |   |   | • |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | Arg Val | l Tyr | Ser   | Asp   | Leu      | Ser   | Ser  | Ile    | Cys        | Arg   | Ala      | Ala  | Val   | His   |   |   |   |   |    |   | 22  |
|     | ٠.      | -     |       | 440   |          |       |      |        | 445        |       |          |      |       | 450   |   |   |   |   |    |   |     |
| •   |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   | •   |
|     | Ala Gly | . Val | Val   | Ara   | Asn      | His   | Glv  | Glv    | Tvr        | Val   | Asp      | Val  | Met   | Pro   |   |   |   |   |    |   |     |
| • * |         | y var | Vul   | 455   | 11011    |       | 1    | 0_3    | 460        |       |          |      |       | 465   |   |   |   |   |    |   |     |
|     |         |       |       | 433   |          |       |      |        | 400        |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       | T     | m\       | m     |      | 77.    |            | Dha   | C1:5     | 7 cn |       | Tla   |   |   | • |   |    |   |     |
|     | Val Asp | э гуѕ | Arg   |       |          | туг   | TTE  | Ala    |            |       | GIII     | ASII | СТА   |       |   |   |   |   |    |   |     |
|     |         |       |       | 470   |          |       |      |        | 475        |       | ٠.       |      |       | 480   |   |   |   |   |    |   | * . |
|     |         |       |       |       | -        |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
| •   | Phe Ser | r Glu | Ser   | Leu   | Gln      | Asn   | Pro  | Pro    | Gly        | , Gly | Lys      | Ala  | Phe   |       |   |   |   |   |    |   |     |
|     |         |       |       | 485   |          |       |      |        | 490        | )     |          |      |       | 495   |   |   |   |   |    |   |     |
| ,   |         | •     |       |       |          |       |      |        |            |       |          |      | •     |       |   |   |   |   |    |   |     |
|     | Val Ph  | e Ala | Val   | Val   |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       | 500   |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       | - 20  |       |          |       |      |        |            |       |          |      |       |       |   |   |   | • |    |   |     |
|     | <210> 3 | 64    |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   | 4, |   |     |
|     | <211> 2 |       |       |       |          |       |      |        |            |       |          |      |       | :     | • |   |   |   |    |   |     |
|     | <211> 2 |       |       |       |          |       |      |        |            |       |          | 8 .  | -     |       |   |   |   |   | •  |   |     |
|     |         |       |       | •     |          | _     |      |        |            |       |          |      |       | ·     |   |   |   |   |    |   |     |
|     | <213> A | rtiti | cıaı  | Seq   | luenc    | :e    |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         | ,     |       |       |          |       |      |        |            |       |          | •    |       |       |   |   |   |   |    |   |     |
| ·   | <220>   |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | <223> S | ynthe | tic   | olig  | onuc     | cleot | ide  | prob   | oe -       |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
| ·   | <400> 3 | 64    |       |       |          |       |      |        |            |       | •        |      |       |       |   |   |   |   |    |   |     |
|     | ggacag  |       | taga  | ıaαca | ica c    | taa   | 24   |        |            |       |          | •    | ٠.    |       |   |   |   |   |    | : |     |
|     | 99      |       | ~555  | , 5   |          | 55    |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | <210> 3 | 65    |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    | • |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | <211> 2 |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   | •  |   |     |
| •   | <212> D |       |       |       |          | •     |      |        |            |       |          |      | ,     |       |   |   |   |   |    |   |     |
|     | <213> A | rtifi | cial  | Sec   | queno    | ce    |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
| •   |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     | <220>   |       |       |       |          |       |      |        |            |       |          |      |       |       | 1 |   |   |   |    |   |     |
|     | <223> S | ynthe | etic  | olic  | gonu     | cleo  | tide | prol   | эе         |       |          |      |       |       |   |   |   |   |    |   |     |
| •   | _       | _     | _     |       |          |       |      | -      |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       |       |          |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       |       | •        |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
|     |         |       |       | .,    | •        |       |      |        |            |       |          |      |       |       |   |   |   |   |    |   |     |
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<sup>&</sup>lt;211> 111

<sup>&</sup>lt;212> PRT

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 Pro His Cys Glu Glu Lys Met Val Ile Ile Thr Thr Lys Ser Val
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Ser Pro Pro Thr Gly Glu Arg Arg Phe Gln Pro Pro Glu Pro Pro 65 70 75

Ser Ser Trp Thr Gly Ile Arg Asn Thr Thr Gln Phe Ala Ala Val

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Gln Asp Gln Asn Glu Asp Cys Leu Tyr Leu Asn Ile Tyr Val Pro 125 130 135

Thr Glu Asp Gly Ala Asn Thr Lys Lys Asn Ala Asp Asp Ile Thr 140 145 150

|   | Ser | Asn   | Asp   | Arg   | Gly                      | Glu | Asp   | Glu | Asp   | Ile        | His      | Asp   | Gln  | Asn   | Ser        |          |     |    | ٠ |   | ,        |
|---|-----|-------|-------|-------|--------------------------|-----|-------|-----|-------|------------|----------|-------|------|-------|------------|----------|-----|----|---|---|----------|
|   |     |       |       |       | 155                      |     |       |     |       | 160        |          |       |      |       | 165        |          |     |    |   |   |          |
|   | Lys | Lys   | Pro   | Val   | Met<br>170               | Val | Tyr   | Ile | His   | Gly<br>175 |          | Ser   | Tyr  | Met   | Glu<br>180 |          |     |    |   |   |          |
|   | Gly | Thr   | Gly   | Asn   | Met<br>185               | Ile | Asp   | Gly | Ser   | Ile<br>190 | Leu      | Ala   | Ser  | Tyr   | Gly<br>195 |          |     |    |   |   |          |
|   | Asn | Val   | Ile   | Val   | Ile<br>200               | Thr | Ile   | Asn | Tyr   | Arg<br>205 | Leu      | Gly   | Ile  | Leu   | Gly<br>210 |          |     |    |   |   |          |
|   | Phe | Leu   | Ser   | Thr   | Gly<br>215               | Asp | Gln   | Ala | Ala   | Lys<br>220 | Gly      | Asn   | Tyr  | Gly   | Leu<br>225 |          |     |    |   |   |          |
| · | Leu | Asp   | Gln   | Ile   | Gln<br>230               | Ala | Leu   | Arg | Trp   | Ile<br>235 | Glu      | Glu   | Asn  | Val   | Gly<br>240 |          |     |    |   |   |          |
|   | Ala | Phe   | Gly   | Gly   | Asp<br>245               | Pro | Lys   | Arg | Val   | Thr<br>250 |          | Phe   | Gly  | Ser   | Gly<br>255 | •        |     |    |   |   |          |
|   | Ala | Gly   | Ala   | Ser   | Cys<br>260               | Val | Ser   | Leu | Leu   | Thr<br>265 | Leu<br>: | Ser   | His  | Tyr   | Ser<br>270 |          |     |    | - |   |          |
|   | Glu | Gly   | Leu   | Phe   | Gln<br>275               | Lys | Ala   | Ile | Ile   | Gln<br>280 |          | Gly   | Thr  | Ala   | Leu<br>285 |          |     |    |   |   |          |
|   | Ser | Ser   | Trp   | Ala   | Val<br>290               | Asn | Tyr   | Gln | Pro   | Ala<br>295 |          | Tyr   | Thr  | Arg   | Ile<br>300 | i        | • . | ř  |   |   |          |
|   | Leu | Ala   | Asp   | Lys   | Val<br>305               |     | Cys   | Asn | Met   | Leu<br>310 |          | Thr   | Thr  | Asp   | Met<br>315 |          |     |    |   |   |          |
|   | Val | Glu   | Cys   | Leu   | Arg<br>320               | Àsn | Lys   | Asn | Tyr   | Lys<br>325 |          | Leu   | I·le | Gln   | Gln<br>330 |          |     | ٠. |   |   |          |
|   | Thr | Ile   | . Thr | Pro   | Ala<br>335               |     | Tyr   | His | Ile   | Ala<br>340 |          | Gly   | Pro  | Val   | Ile<br>345 |          |     |    | , |   |          |
|   | Asp | Gly   | Asp   | Val   | Ile<br>35 <sub>,</sub> 0 |     | Asp   | Asp | Pro   | Gln<br>355 |          | Leu   | Met  | Glu   | Gln<br>360 | ,        |     |    |   | - |          |
|   | Gly | Glu   | , Phe | Leu   | Asn<br>365               |     | Asp   | Ile | Met   | Leu<br>370 |          | v Val | Asn  | Gln   | Gly<br>375 |          |     |    |   |   | <i>:</i> |
|   | Glu | Gly   | / Leu | Lys   | Phe<br>380               |     | Asp   | Gly | , Ile | Val<br>385 |          | Asn   | Glu  | Asp   | Gly<br>390 |          |     | *  |   |   | f        |
|   | Va] | Thr   | Pro   | Asn   | Asp<br>395               |     | Asp   | Phe | Ser   | Val<br>400 |          | : Asn | Phe  | val   | Asp<br>405 |          |     |    |   |   | · .      |
|   | Asr | ı Lev | ı Tyr | Gly   | Tyr<br>410               |     | Glu   | Gly | , Lys | Asp<br>415 |          | Leu   | Arç  | g Glu | Thr<br>420 | •<br>• • |     |    |   |   | · .      |
|   | Ile | e Lys | s Phe | e Met | Tyr<br>425               |     | : Asp | Trp | Ala   | Asp<br>430 |          | s Glu | Asr  | ı.Pro | Glu<br>435 |          |     |    | • |   |          |
| £ | •   |       |       |       |                          | •   |       | ٠   |       |            |          |       |      | •     | •          |          |     |    |   |   |          |
|   |     |       |       |       |                          |     |       |     |       |            | ŕ        |       |      |       |            |          |     |    |   |   |          |
|   |     |       | •     |       |                          | *   |       |     |       |            |          | •     |      |       |            |          |     | ٠  |   |   |          |

|   | Thr | Arg   | Arg   | Lys   | Thr<br>440 | Leu | Val | Ala     | Leu | Phe<br>445  |          | Asp   | His | Gln     | Trp<br>450   |   |   |      |      |
|---|-----|-------|-------|-------|------------|-----|-----|---------|-----|-------------|----------|-------|-----|---------|--------------|---|---|------|------|
|   | Val | Ala   | Pro   | Ala   | Val<br>455 | Ala | Ala | Asp     | Leu | His<br>460  | Ala      | Gln   | Tyr | Gly     | Ser<br>465   |   |   |      |      |
|   | Pro | Thr   | Tyr   | Phe   | Tyr<br>470 | Ala | Phe | Tyr     | His | His<br>475  | Cys      | Gln   | Ser | Glu     | Met<br>480   |   |   |      |      |
|   | Lys | Pro   | Ser   | Trp   | Ala<br>485 | Asp | Ser | Ala     | His | Gly<br>490  | Asp      | Glu   | Val |         | Tyr<br>495   |   |   |      | *    |
|   | Val | Phe   | Gly   | Ile   | Pro<br>500 | Met | Ile | Gly     | Pro | Thr<br>505  | Glu      | Leu   | Phe | Ser     | Cys<br>510   |   |   |      |      |
|   | Asn | Phe   | Ser   | Lys   | Asn<br>515 | Asp | Val | Met<br> | Leu | Ser<br>_520 | Ala      | Val   | Val | Met<br> | Thr<br>525_  |   |   | <br> |      |
| ٠ | Tyr | Trp   | Thr   | Asn   | Phe<br>530 | Ala | Lys | Thr     | Gly | Asp<br>535  | Pro      | Asn   | Gln | Pro     | Val<br>540   |   |   |      |      |
| • | Pro | Gln   | Asp   | Thr   | Lys<br>545 | Phe | Ile | His     | Thr | Lys<br>550  | Pro      | Asn   | Arg | Phe     | Glu<br>555   |   | * |      |      |
|   | Glu | Val   | Ala   | Trp   | Ser<br>560 | Lys | Tyr | Asn     | Pro | Lys<br>565  | Asp      | Gln   | Leu | Tyr     | Leu<br>570   |   |   |      | 30 ° |
|   | His | .Ile  | Gly   | Leu   | Lys<br>575 | Pro | Arg | Val     | Arg | Asp<br>580  |          | Tyr   | Arg | Ala     | Thr<br>585   |   |   |      |      |
|   | Lys | Val   | . Ala | Phe   | Trp<br>590 | Leu | Glu | Leu     | Val | Pro<br>595  |          | Leu   | His | Asn     | Leu<br>600   |   |   |      |      |
|   | Asn | ,Glu  | ılle  | Phe   | Gln<br>605 | Tyr | Val | Ser     | Thr | Thr<br>610  |          | Lys   | Val | . Pro   | Pro<br>615   |   |   |      | •    |
|   | Pro | Asp   | Met   | Thr   | Ser<br>620 | Phe | Pro | Tyr     | Gly | Thr<br>625  |          | Ārg   | Ser | Pro     | 630          |   |   |      |      |
|   | Lys | : Ile | Trp   | Pro   | Thr<br>635 |     | Lys | Arg     | Pro | Ala<br>640  |          | Thr   | Pro | Ala     | Asn<br>645   |   |   |      |      |
|   | •   |       |       |       | 650        |     |     |         |     | 655         | <b>5</b> |       |     |         | Asp<br>660   |   |   |      |      |
|   |     |       |       |       | 665        |     |     |         |     | 670         | )        |       |     |         | 1 Leu<br>675 |   |   |      |      |
|   |     |       |       |       | 680        |     |     | ٠.      | *   | 685         | 5 .      |       |     |         | 690          |   |   |      |      |
|   |     |       |       |       | 695        |     | •   |         |     | 700         | )        |       |     |         | 705          |   |   |      | · ·  |
|   | Gli | u Thi | r His | s Arg | 710        |     | Ser | r Pro   | Glr | 71:         |          | n Thi | Thi | r Ası   | 720          | • |   |      |      |
|   |     |       |       |       |            |     |     |         | ٠   |             |          |       |     |         |              |   |   |      | •    |
|   |     |       |       |       |            |     |     |         |     |             |          |       | •   |         |              |   |   |      |      |

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                                     745 .
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<sup>&</sup>lt;211> 348

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|         |     |       |       |            |     |      |     |       | . •            |     |       |       |       |            |   |   |   |   |    |  |
|---------|-----|-------|-------|------------|-----|------|-----|-------|----------------|-----|-------|-------|-------|------------|---|---|---|---|----|--|
| Leu     | Leu | Leu   | Gly   | Ser<br>35  | Gly | Gln  | Gly | Pro   | Gln.<br>40     | Gln | Val   | Gly   | Ala   | Gly<br>45  |   |   |   |   |    |  |
| Gln     | Thr | Phe   | Glu   | Tyr<br>50  | Leu | Lys  | Arg | Glu   | His<br>55      | Ser | Leu   | Ser   | Lys   | Pro<br>60  |   |   |   |   | ٠. |  |
| Tyr     | Gln | Gly   | Val   | Gly<br>65  | Thr | Gly  | Ser | Ser   | Ser<br>70      | Leu | Trp   | Asn   | Leu   | Met<br>75  |   |   |   |   |    |  |
| Gly     | Asn | Ala   |       | Val<br>.80 | Met | Thr  | Gln | Tyr   | Ile<br>85      | Arg | Leu   | Thr   | Pro   | Asp<br>90  |   |   |   |   |    |  |
| Met     | Gln | Ser   | Lys   | Gln<br>95  | Gly | Ala  | Leu | Trp   | Asn<br>100     | Arg | Val   | Pro   | Cys   | Phe<br>105 | , |   |   |   |    |  |
| <br>Leu | Arg | Asp   | Trp   | Glu<br>110 | Leu | Gln  | Val | His   | Phe<br>115     | Lys | Ile   | His   | Gly   | Gln<br>120 |   |   |   |   |    |  |
| Gly     | Lys | Lys   | Asn   | Leu<br>125 | His | Gly  | Asp | Gly   | Leu<br>130     | Ala | Ile   | Trp   | Tyr   | Thr<br>135 |   |   |   | • |    |  |
| Lys     | Asp | Arg   | Met   | Gln<br>140 | Pro | Gly  | Pro | Val   | Phe<br>145     | Glý | Asn   | Met   | Asp   | Lys<br>150 |   | • |   |   |    |  |
| Phe     | Val | Gly   | Leu   | Gly<br>155 | Val | Phe  | Val | Asp   | Thr<br>160     | Tyr | Pro   | Asn   | Glu   | Glu<br>165 |   |   |   |   |    |  |
| Lys     | Gln | Gln   | Glu   | Arg<br>170 | Val | Phe  | Pro | Tyr   | Ile<br>175     | Ser | Ala   | Met   | Val   | Asn<br>180 |   |   |   |   |    |  |
| Asn     | Gly | Ser   | Leu   | Ser<br>185 | Tyr | Asp  | His | Glu   | Arg<br>190<br> | Asp | Gly   | Arg   | Pro   | Thr<br>195 |   |   |   | • |    |  |
| Glu     | Leu | Gly   | Gly   | Cys<br>200 |     | Ala  | Ile | Val   | Arg<br>205     | Asn | Leu   | His   | Tyr   | Asp<br>210 |   |   |   |   |    |  |
| Thr     | Phe | Leu   | Val   | Ile<br>215 | Arg | Tyr  | Val | Lys   | Arg<br>220     | His | Leu   | Thr   | Ile   | Met<br>225 |   |   |   |   |    |  |
| Met     | Asp | Ile   | Asp   | Gly<br>230 |     | His  | Glu | Trp   | Arg<br>235     | Asp | Cys   | Ile   | Glu   | Val<br>240 | ÷ |   |   | , |    |  |
| Pro     | Gly | Val   | . Arg | Leu<br>245 |     | Arg  | Gly | Tyr   | Tyr<br>250     |     | Gly   | Thr   | Ser   | Ser<br>255 |   |   | • |   |    |  |
| Ile     | Thr | Gly   | Asp   | Leu<br>260 |     | Asp  | Asn | His   | 265            |     | Ile   | Ser   | Leu   | Lys<br>270 |   |   |   |   |    |  |
| Leu     | Phe | e Glu | . Leu | Thr<br>275 |     | Glu  | Arg | Thr   | 280            | Glu | Glu   | Glu   | Lys   | 285        |   |   |   |   |    |  |
| His     | Arg | Asp   | Val   | Phe<br>290 |     | ·Pro | Ser | · Val | Asp<br>295     | Asn | Met   | Lys   | : Leu | Pro<br>300 |   |   |   |   |    |  |
| Glu     | Met | Thi   | Ala   | 305        |     | Pro  | Pro | Leu   | Ser<br>310     |     | / Let | ı Ala | a Let | Phe 315    |   | ٠ |   |   |    |  |

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| gatt                             | ctct           | gt t   | gtca  | tcgg       | c at | tcca | actt | ttt | ctct       | ttg | tttt | tgtc | ca 3             | 100        |   |
|----------------------------------|----------------|--------|-------|------------|------|------|------|-----|------------|-----|------|------|------------------|------------|---|
| gtgt                             | tgca           | itt t  | gaat  | atġt       | c tg | tttc | tata | aat | aaat       | ttt | ttaa | gaat | aa 3             | 150        |   |
| <2102<br><2112<br><2122<br><2132 | > 480<br>> PRT | )<br>[ | npien | ıs         |      |      |      |     |            |     |      | ·.   |                  | * •        |   |
| <400                             | > 385          | 5 .    |       |            |      |      |      |     |            |     |      |      |                  |            |   |
| Met<br>1                         | Leu            | Phe    | Arg   | Asn<br>5   | Arg  | Phe  | Leu  | Leu | Leu<br>10. | Leu | Ala  | Leu  | Ala              | Ala<br>15  |   |
| Leu                              | Leu            | Ala    | Phe   | Val<br>20  | Ser  | Leu  | Ser  | Leu | Gln<br>25  | Phe | Phe  | His  | Leu              | Ile<br>30  |   |
| Pro                              |                | Ser    |       |            |      |      | Gly  | Met | Ser<br>40  | Ser | Lys  | Ser  | Arg              | Lys<br>45  | - |
| Arg                              | Ile            | Met    | Pro   | Asp<br>50  | Pro  | Val  | Thr  | Glu | Pro<br>55  | Pro | Val  | Thr  | Asp              | Pro<br>60  |   |
| Val                              | Tyr            | Glu    | Ala   | Leu<br>65  | Leu  | Tyr  | Cys  | Asn | Ile<br>70  | Pro | Ser  | Val  | Ala              | Glu<br>75  |   |
| Arg                              | Ser            | Met    | Glu   | Gly<br>80  | His  | Ala  | Pro  | His | His<br>85  | Phe | Lys  | Leu  | Val <sup>.</sup> | Ser<br>90  |   |
| Val                              | His            | Val    | Phe   | Ile<br>95  | Arg  | His  | Gly  | Asp | Arg<br>100 | Tyr | Pro  | Leu  | Tyr              | Val<br>105 |   |
| Ile                              | Pro            | Lys    | Thr   | Lys<br>110 | Arg  | Pro  | Glu  | Ile | Asp<br>115 | Cys | Thr  | Leu  | Val              | Ala<br>120 |   |
| Asn                              | Arg            | Lys    | Pro   | Tyr<br>125 |      | Pro  | Lys  | Leu | Glu<br>130 | Ala | Phe  | Ile  | Ser              | His<br>135 |   |
| Met                              | Ser            | Lys    | Gly   | Ser<br>140 | Gly  | Ala  | Ser  | Phe | Glu<br>145 | Ser | Pro  | Leu  | Asn              | Ser<br>150 |   |
| Leu                              | Pro            | Leu    | Tyr   | Pro<br>155 | Asn  | His  | Pro  | Leu | Cys<br>160 | Glu | Met  | Gly  | Glu              | Leu<br>165 |   |
| Thr                              | Gln            | Thr    | Gly   | Val<br>170 | Val  | Glņ  | His  | Leu | Gln<br>175 |     | Gly  | Gln  | Lėu              | Leu<br>180 |   |
| Arg                              | Asp            | Ile    | Tyr   | Leu<br>185 | Lys  | Lys  | His  | Lys | Leu<br>190 | Leu | Pro  | Asn  | Asp              | Trp<br>195 |   |
| Ser                              | Ala            | Asp    | Gln   | Leu<br>200 |      | Leu  | Glu  | Thr | Thr<br>205 | Gly | Lys  | Ser  | Arg              | Thr<br>210 |   |
| Leu                              | Gln            | Ser    | Gly   | Leu<br>215 |      | Leu  | Leu  | Tyr | Gly<br>220 | Phe | Leu  | Pro  | Asp              | Phe<br>225 |   |
| Asp                              | Trp            | Lys    | Lys   | Ile<br>230 |      | Phe  | Arg  | His | Gln<br>235 | Pro | Ser  | Ala  | Leu              | Phe<br>240 |   |

| Суѕ  | Ser   | Gly   | Ser   | Cys<br>245 | Tyr | Cys   | Pro | Val | Arg.<br>250 | Asn   | Gln   | Tyr   | Leu   | Glu<br>255 |
|------|-------|-------|-------|------------|-----|-------|-----|-----|-------------|-------|-------|-------|-------|------------|
| Lys  | Glu   | Gln   | Arg   | Arg<br>260 | Gln | Tyr   | Leu | Leu | Arg<br>265  | Leu   | Lys   | Asn   | Ser   | Gln<br>270 |
| Leu  | Glu   | Lys   | Thr   | Tyr<br>275 | Gly | Glu   | Met | Ala | Lys<br>280  | Ile   | Val   | Asp   | Val   | Pro<br>285 |
| Thr  | Lys   | Gln   | Leu   | Arg<br>290 | Ala | Ala   | Asn | Pro | Ile<br>295  | Asp   | Ser   | Met   | Leu   | Cys<br>300 |
| His  | Phe   | Cys   | His   | Asn<br>305 | Val | Ser   | Phe | Pro | Cys<br>310  | Thr   | Arg   | Asn   | Gly   | Cys<br>315 |
| Val  | Asp   | Met   | Glu   | His<br>320 | Phe | Lys   | Val | Ile | Lys<br>325  | Thr   | His   | Gln   | Ile   | Glu<br>330 |
| Asp  | Glu   | Arg   | Glu   | Arg<br>335 | Arg | Glu   | Lys | Lys | Leu<br>340  | Tyr   | Phe   | Gly   | Tyr   | Ser<br>345 |
| Leu  | Leu   | Gly   | Ala   | His<br>350 | Pro | Ile   | Ļeu | Asn | Gln<br>355  | Thr   | Ile   | Gly   | Arg   | Met<br>360 |
| Gln  | Arg   | Ala   | Thr   | Glu<br>365 | Gly | Arg   | Lys | Glu | Glu<br>370  |       | Phe   | Ala   | Leu   | Tyr<br>375 |
| Ser  | Ala   | His   | Asp   | Val<br>380 | Thr | Leu   | Ser | Pro | Val<br>385  | Leu   | Ser   | Ala   | Leu   | Gly<br>390 |
| Leu  | Ser   | Glu   | Ala   | Arg<br>395 |     | Pro   | Arg | Phe | Ala<br>400  | Ala   | Arg   | Leu   | Ile   | Phe<br>405 |
| Glu  | Leu   | Trp   | Gln   | Asp<br>410 |     | Glu   | Lys | Pro | Ser<br>415  |       | His   | Ser   | Val   | Arg<br>420 |
| Ile  | Leu   | Tyr   | Asn   | Gly<br>425 |     | . Asp | Val | Thr | Phe 430     | His   | Thr   | Ser   | Phe   | Cys<br>435 |
| Gln  | Asp   | His   | His   | Lys<br>440 |     | , Ser | Pro | Lys | Pro<br>445  |       | Cys   | Pro   | Leu   | Glu<br>450 |
| Asn  | Leu   | ı Val | . Arg | Phe<br>455 |     | Lys   | arg | Asp | Met<br>460  | : Phe | . Val | Ala   | Leu   | Gly<br>465 |
| Gly  | Ser   | Gly   | Thr   | 470        |     | Туг   | Asp | Ala | Cys<br>475  |       | Arg   | g Glu | ı Gly | Phe 480    |
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<sup>&</sup>lt;210> 390

<sup>&</sup>lt;211> 916

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 390

|   |   | Met<br>1 | Ile   | Pro | Ala     | Arg<br>5   | Leu      | His           | Arg | Asp   | Tyr<br>. 10. |     | Ġly   | Leu   | Val   | Leu<br>15  |   |    |               | • |                 |     |
|---|---|----------|-------|-----|---------|------------|----------|---------------|-----|-------|--------------|-----|-------|-------|-------|------------|---|----|---------------|---|-----------------|-----|
|   |   | Leu      | Gly   | Ile | Leu     | Leu<br>20  | Gly      | Thr           | Leu | Trp   | Glu<br>25    | Thr | Gly   | Cys   | Thr   | Gln<br>30  |   |    |               |   |                 |     |
|   |   | Ile      | Arg   | Tyr | Ser     | Val<br>35  | Pro      | Glu           | Glu | Leu   | Glu<br>40    | Lys | Gly   | Ser   | Arg   | Val<br>45  |   |    |               |   |                 |     |
|   |   | Gly      | Asp   | Ile | Ser     | Arg<br>50  | Asp      | Leu           | Gly | Leu   | Glu<br>55    |     | Arg   | Glu   | Leu   | Ala<br>60  | • |    |               | • |                 | 0   |
|   |   | Glu      | Arg   | Gly | Val     | Arg<br>65  | Ile      | Ile           | Pro | Arg   | Gly<br>70    | Arg | Thr   | Gln   | Leu   | Phe<br>75  |   |    |               | ÷ |                 |     |
|   |   | Ala      | Leu   | Asn | Pro<br> | Arg<br>80  | Ser<br>- | Gly<br>       | Ser | Leu   | Val<br>85    | Thr | Ala   | Gly   | Arg   | Ile<br>90  |   |    | <del></del> - |   |                 |     |
|   |   | Asp,     | Arg   | Glu |         | Leu<br>95  | Cys      | Met           | Gly | Ala   | Ile<br>100   | Lys | Cys   | Gln   | Leu   | Asn<br>105 |   |    |               |   |                 |     |
|   |   |          | ,     |     |         | Met<br>110 | • .      |               |     |       | 115          |     |       |       |       | 120        |   |    |               |   |                 |     |
|   |   |          |       | ,*  |         | Asp<br>125 |          |               |     |       | 130          | ,   |       |       |       | 135        |   |    | ·             |   |                 | اد. |
|   | • |          |       |     |         | Ile<br>140 |          |               |     |       | 145          |     |       |       |       | 150        |   |    |               |   |                 |     |
|   |   |          |       |     |         | Pro<br>155 |          |               |     |       | 160          |     |       |       |       | 165        |   |    |               |   |                 |     |
|   |   |          |       |     |         | Tyr<br>170 |          |               |     |       | 175          |     | 1     |       |       | 180        |   |    |               |   |                 |     |
|   |   |          |       |     |         | Gly<br>185 |          |               |     |       | 190          |     |       |       |       | 195        |   |    |               |   |                 | -)( |
|   |   |          |       |     |         | 200        |          |               |     |       | 205          |     |       |       |       | 210        | · |    |               |   | e in the second |     |
|   |   |          |       |     |         | 215        |          |               |     |       | 220          |     |       |       |       | Thr<br>225 |   | ٠. |               |   |                 | · . |
|   |   |          |       |     |         | 230        |          |               |     |       | 235          |     |       | ,     |       | 240        |   |    |               |   |                 |     |
| • |   |          |       |     |         | 245        |          |               |     |       | 250          |     |       | ٠.    |       | 255        |   |    |               |   |                 |     |
|   |   | *        |       | _   |         | 260        |          |               | •   |       | 265          |     |       |       |       | Asp 270    |   |    | •             |   |                 |     |
|   |   | 910      | , сту | val | . noil  | 275        |          | . <b>v</b> al | ria | ı ıyı | 280          |     | , ALG | . TAT | . val | Asp<br>285 |   |    |               |   |                 |     |
|   |   |          |       |     |         |            |          |               |     |       |              |     |       |       |       |            |   |    |               |   |                 |     |

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|     | Asp | Lys | Ala | Ala | Gln<br>290 | Val | Phe | Lys | Leu | Asp<br>295 |     | Asn | Ser | Gly     | Thr<br>300 |    | ٠.   |    |   |   |
|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|---------|------------|----|------|----|---|---|
|     | Ile | Ser | Thr | Ile | Gly<br>305 | Glu | Leu | Asp | His | Glu<br>310 | Glu | Ser | Gly | Phe     | Tyr<br>315 |    |      |    |   |   |
|     | Gln | Met | Glu | Val | Gln<br>320 | Ala | Met | Asp | Asn | Ala<br>325 | Gly | Tyr | Ser | Ala     | Arg<br>330 |    |      |    |   |   |
| *   | Ala | Lys | Val | Leu | Ile<br>335 | Thr | Val | Leu | Asp | Val<br>340 | Asn | Asp | Asn | Ala     | Pro<br>345 |    |      | ,  |   |   |
| •   | Glu | Val | Val | Leu | Thr<br>350 | Ser | Leu | Ala | Ser | Ser<br>355 | Val | Pro | Glu | Asn     | Ser<br>360 |    |      |    |   |   |
|     | Pro | Arg | Gly | Thr | Leu<br>365 | Ile | Ala | Leu | Leu | Asn<br>370 | Val | Asn | Asp | Gln<br> | Asp<br>375 |    | <br> | :_ |   |   |
|     | Ser | Glu | Glu |     | Gly<br>380 | Gln | Val | Ile | Cys | Phe<br>385 | Ile | Gln | Gly | Asn     | Leu<br>390 |    |      |    |   |   |
|     | ••  |     |     |     | Glu<br>395 |     |     |     |     | 400        |     |     |     |         | 405        |    |      |    |   |   |
|     | Thr | Asp | Ile | Val | Leu<br>410 | Asp | Arg | Glu | Gln | Val<br>415 | Pro | Ser | Tyr | Asn     | 11e<br>420 |    |      |    |   |   |
|     |     |     |     |     | Thr<br>425 |     |     |     |     | 430        |     |     | ٠   |         | 435        |    | ٠.,  |    |   |   |
|     |     |     |     |     | Leu<br>440 |     |     |     |     | 445        |     |     |     |         | 450<br>·   |    | . 4  |    |   |   |
|     |     |     |     | ,   | Ala<br>455 |     |     |     |     | 460        |     |     |     | :       | 465        |    |      |    | • |   |
|     |     |     |     |     | Ser<br>470 |     |     |     |     | 475        |     |     |     |         | 480        |    |      |    | • |   |
|     | •   |     | . 4 |     | 485        |     |     |     |     | 490        |     |     |     |         | Thr<br>495 |    |      |    |   |   |
|     |     |     |     |     | 500        |     |     |     |     | 505        |     |     |     |         | Asp 510    | •  | •    |    |   |   |
|     |     |     |     |     | 515        |     |     |     |     | 520        |     |     |     |         | Phe 525    |    |      |    |   |   |
| , · |     |     |     |     | 530        | -   |     |     |     | 535        |     |     |     |         | 540        |    |      |    |   | * |
|     |     |     |     |     | 545        | •   | •   | •   |     | 550        |     |     |     |         | 555        |    |      |    |   |   |
|     | Asn | Asp | Asn | Ala | Pro<br>560 |     | Ile | Leu | Tyr | Pro<br>565 |     | Leu | Pro | Thr     | 570        | •• |      |    |   |   |

- •

|    |     |     |       |     |            |     |     |      |     |             |     |     |     |     |            |     |                |   |   |     | •   |
|----|-----|-----|-------|-----|------------|-----|-----|------|-----|-------------|-----|-----|-----|-----|------------|-----|----------------|---|---|-----|-----|
|    | Gly | Ser | Thr   | Gly | Val<br>575 | Glu | Leu | Ala  | Pro | Arg<br>580  |     | Ala | Glu | Pro | Gly<br>585 |     | •              |   |   | ٠   |     |
|    | Tyr | Leu | Val   | Thr | Lys<br>590 | Val | Val | Ala  | Val | Asp<br>595  |     | Asp | Ser | Gly | Gln<br>600 |     |                |   |   |     |     |
|    | Asn | Ala | Trp   | Leu | Ser<br>605 | Tyr | Arg | Leu  | Leu | Lys<br>610  | Ala | Ser | Glu | Pro | Gly<br>615 |     |                |   |   |     |     |
|    | Leu | Phe | Ser   | Val | Gly<br>620 | Leu | His | Thr  | Gly | Glu<br>625  | Val | Arg | Thr | Ala | Arg<br>630 |     |                |   |   |     |     |
| ٠. | Ala | Leu | Leu   | Asp |            | Asp | Ala | Leu  | Lys |             | Ser | Leu | Val | Vaİ | Ala<br>645 |     |                |   |   |     |     |
|    | Val | Gln | Asp   | His | Gly        | Gln | Pro | Pro  | Leu | Ser         | Ala | Thr | Val | Thr | Leu        |     |                |   |   |     | •   |
|    | :   |     |       |     | 650        |     |     |      |     | 655         |     |     |     |     | 660        |     | <del>.</del> - |   |   | - ; |     |
|    | Thr | Val | Ala   | Val | Ala<br>665 | Asp | Ser | I·le | Pro | Gln<br>670  | Val | Leu | Ala | Asp | Leu<br>675 |     |                |   |   |     |     |
|    | Gly | Ser | Leu   | Glu | Ser<br>680 | Pro | Ala | Asn  |     | Glu<br>.685 |     | Ser | Asp | Leu | Thr<br>690 | •   |                |   |   |     | ·.  |
|    | Leu | Tyr | Leu   | Val | Val<br>695 | Ala | Val | Ala  | Ala | Val<br>700  |     | Cys | Val | Phe | Leu<br>705 |     |                |   |   | ٠.  | . 9 |
|    | Ala | Phe | Val   | Ile | Leu<br>710 | Lėu | Leu | Ala  | Leu | Arg<br>715  |     | Arg | Arg | Trp | His<br>720 |     |                |   |   |     | ~ . |
| •  | Lys | Ser | Arg   | Leu | Leu<br>725 |     | Ala | Ser  | Gly | Gly<br>730  |     | Leu | Thr | Gly | Ala<br>735 |     |                |   |   |     | •   |
|    | Pro | Aļa | Ser   | His | Phe        |     | Gly | Val  | Asp | Gly<br>745  |     | Gln | Ala | Phe | Leu<br>750 |     |                |   | ٠ |     | . = |
|    | Gln | Thr | Tyr   | Ser | His        |     | Val | Ser  | Leu | Thr         | Thr | Asp | Ser | Arg |            |     |                |   | • |     |     |
| •  | Ser | His | Leu   | Ile | 755<br>Phe |     | Gln | Pro  | Asn |             | Ala | Asp | Met | Leu | Val        |     |                |   |   |     |     |
|    |     |     |       |     | 770        |     |     |      |     | 775         |     |     |     |     | 780        |     |                |   |   |     |     |
|    | Ser | Gln | Glu   | Ser | Phe<br>785 |     | Lys | Ser  | Glu | Pro<br>790  |     | Leu | Leu | Ser | Gly<br>795 |     |                |   | , |     |     |
|    | Asp | Ser | Vaļ   | Phe | Ser<br>800 |     | Asp | Ser  | His | Gly<br>805  |     | Ile | Glu | Val | Ser<br>810 | . * |                |   |   |     |     |
|    | Leu | Tyr | . Gln | Ile | Phe<br>815 |     | Leu | Phe  | Phe | Phe<br>820  |     | Cys | Ser | Val | Ser<br>825 |     |                |   |   | :   |     |
|    | Gln | Ala | Gly   | Val | Gln<br>830 |     | Tyr | Asp  | His | Ser<br>835  |     | Leu | Arg | Pro | Gln<br>840 |     |                |   |   |     |     |
|    | Thr | Pro | Arg   | Leu | Lys<br>845 |     | Leu | Ser  | His | Leu<br>850  |     | Leu | Arg | Cys | Asn<br>855 |     |                | • |   |     |     |
|    |     |     |       |     |            |     |     |      | ٠   |             |     |     |     |     |            |     |                |   |   |     |     |
|    |     |     |       |     |            |     |     |      |     |             |     |     |     |     |            |     |                |   |   |     |     |
|    |     |     |       |     |            |     |     |      |     |             |     |     | •   |     |            |     |                | _ |   |     |     |
|    |     |     |       |     |            |     |     |      |     |             |     |     |     |     |            |     |                | - |   |     |     |

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Asp Lys Val Leu Gly Gly His Glu Cys Gln Pro His Ser Gln Pro 35 40 45

Trp Gln Ala Ala Leu Phe Gln Gly Gln Gln Leu Leu Cys Gly Gly 50 55 60

Val Leu Val Gly Gly Asn Trp Val Leu Thr Ala Ala His Cys Lys

<sup>&</sup>lt;210> 395

<sup>&</sup>lt;211> 260

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

| Lys                              | Pro          | Lys  | Tyr  | Thr<br>80  | Val  | Arg  | Leu | Gly  | Asp<br>85  | His | Ser  | Leu   | Gln      | Asn<br>90  |
|----------------------------------|--------------|------|------|------------|------|------|-----|------|------------|-----|------|-------|----------|------------|
| Lys                              | Asp          | Gly  | Pro  | Glu<br>95  | Gln  | Glu  | Ile | Pro  | Val<br>100 | Val | Gln  | Ser   | Ile      | Pro<br>105 |
| His                              | Pro          | Cys  | Tyr  | Asn<br>110 | Ser  | Ser  | Asp | Val  | Glu<br>115 | Asp | His  | Asn   | His      | Asp<br>120 |
| Leu                              | Met          | Leu  | Leu  | Gln<br>125 | Leu  | Arg  | Asp | Gln  | Ala<br>130 | Ser | ·Leu | Gly   | Ser      | Lys<br>135 |
| Val                              | Lys          | Pro  | Ile  | Ser<br>140 | Leu  | Ala  | Asp | His  | Cys<br>145 | Thr | Gln  | Pro   | Gly      | Gln<br>150 |
| Lys                              | Cys          | Thr  |      | Ser<br>155 |      | Trp  | Gly | Thr  | Val<br>160 |     | Ser  | Pro   | Arg      | Glu<br>165 |
| Asn                              | Phe          | Pro  | Asp  | Thr<br>170 | Leu  | Asn  | Cys | Ala  | Glu<br>175 | Val | Lys  | Ile   | Phe      | Pro<br>180 |
| Gln                              | Lys          | Lys  | Cys  | Glu<br>185 | Asp  | Ala  | Tyr | Pro  | Gly<br>190 |     | Ile  | Thr   | Asp<br>· | Gly<br>195 |
| Met                              | Val          | Cys  | Ala  | Gly<br>200 | Ser  | Ser  | Lys | Gly  | Ala<br>205 | Asp | Thr  | Cys   | Gln      | Gly<br>210 |
| Asp                              | Ser          | Gly  | Gly  | Pro<br>215 | Leu  | Val  | Cys | Asp  | Gly<br>220 | Ala | Leu  | Gln   | Gly      | Ile<br>225 |
| Thr                              | Ser          | Trp  | Gly  | Ser<br>230 | Asp  | Pro  | Cys | Gly  | Arg<br>235 | Ser | Asp  | Lys   | Pro      | Gly<br>240 |
| Val                              | Tyr          | Thr  | Asn  | Ile<br>245 | ·Cys | Arg  | Tyr | Leu  | Asp<br>250 | Trp | Ile  | Lys   | Lys      | Ile<br>255 |
| Ile                              | Gly          | Ser  | Lys  | Gly<br>260 |      |      |     |      |            |     |      | * . : |          |            |
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| <220<br><223                     |              | nthe | tic  | olig       | onuc | leot | ide | prob | e .        |     |      |       |          |            |
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| Met 1 | Lys | Arg   | Ala  | Ser<br>5   | Ala  | Gly | Gly | Ser   | Arg<br>10   | Leu | Leu | Ala | Trp  | Val<br>15  |
| Leu   | Trp | Leu   | Gln  | Ala<br>20  | Trp  | Gln | Val | Ala   | Ala<br>25   | Pro | Cys | Pro | Gly  | Ala<br>30  |
| Cys   | Val | Cys   | Tyr  | Asn<br>35  | Glu  | Pro | Lys | Val   | Thr<br>40   | Thr | Ser | Cys | Pro  | Gln<br>45  |
| Gln   | Gly | Leu   | Gln  | Ala<br>50  | Val  | Pro | Val | Gly   | Ile<br>55   |     | Ala | Ala | Ser  | Gln<br>60  |
| Arg.  | Ile | .Phe. | Leu. | His<br>65  | -Gly | Asn | Arg | Ile   | -Ser<br>.70 | His | Val | Pro | -Ala | Ala-<br>75 |
| Ser   | Phe | Arg   | Ala  | Cys<br>80  | Arg  | Asn | Leu | Thr   | Ile<br>85   | Leu | Trp | Leu | His  | Ser<br>90. |
| Asn   | Val | Leu   | Ala  | Arg<br>95  | Ile  | Asp | Ala | Ala   | Ala<br>100  | Phe | Thr | Gly | Leu  | Ala<br>105 |
| Leu   | Leu | Glu   | Gln  | Leu<br>110 | Asp  | Leu | Ser | Asp   | Asn<br>115  | Ala | Gln | Leu | Arg  | Ser<br>120 |
| Val   | Asp | Pro   | Ala  | Thr<br>125 | Phe  | His | Gly | Leu   | Gly<br>130  | Arg | Leu | His | Thr  | Leu<br>135 |
| His   | Leu | Asp   | Arg  | Cys<br>140 | Gly  | Leu | Gln | Glu   | Leu<br>145  | Gly | Pro | Gly | Leu  | Phe<br>150 |
| Arg   | Gly | Leu   | Ala  | Ala<br>155 | Leu  | Gln | Tyr | Leu   | Tyr<br>160  |     | Gln | Asp | Asn  | Ala<br>165 |
| Leu   | Gln | Ala   | Leu  | Pro<br>170 | Asp  | Asp | Thr | Phe   | Arg<br>175  |     | Leu | Gly | Asn  | Leu<br>180 |
| Thr   | His | Leu   | Phe  | Leu<br>185 | His  | Gly | Asn | Arg   | Ile<br>190  |     | Ser | Val | Pro  | Glu<br>195 |
| Arg   | Ala | Phe   | Arg  | Gly<br>200 |      | His | Ser | Leu   | Asp<br>205  |     | Leu | Leu | Leu  | His<br>210 |
| Gln   | Asn | Arg   | Val  | Ala<br>215 |      | Val | His | Pro   | His<br>220  |     | Phe | Arg | Asp  | Leu<br>225 |
| Gly   | Arg | Leu   | Met  | Thr<br>230 |      | Tyr | Leu | Phe   | Ala<br>235  |     | Asn | Leu | Ser  | Ala<br>240 |
| Leu   | Pro | Thr   | Glu  | Ala<br>245 |      | Ala | Pro | Leu   | Arg<br>250  |     | Leu | Gln | Tyr  | Leu<br>255 |
| Arg   | Leu | Asn   | Asp  | Asn<br>260 |      | Trp | Val | . Cys | 265         |     | Arg | Ala | Arg  | Pro<br>270 |

Leu Trp Ala Trp Leu Gln Lys Phe Arg Gly Ser Ser Ser Glu Val 275 Pro Cys Ser Leu Pro Gln Arg Leu Ala Gly Arg Asp Leu Lys Arg 290 295 Leu Ala Ala Asn Asp Leu Gln Gly Cys Ala Val Ala Thr Gly Pro 305 Tyr His Pro Ile Trp Thr Gly Arg Ala Thr Asp Glu Glu Pro Leu 325 320 Gly Leu Pro Lys Cys Cys Gln Pro Asp Ala Ala Asp Lys Ala Ser 340 Val. Leu-Glu Pro Gly Arg Pro-Ala Ser-Ala Gly Asn Ala-Leu-Lys 350 Gly Arg Val Pro Pro Gly Asp Ser Pro Pro Gly Asn Gly Ser Gly Pro Arg His Ile Asn Asp Ser Pro Phe Gly Thr Leu Pro Gly Ser 380 385 Ala Glu Pro Pro Leu Thr Ala Val Arg Pro Glu Gly Ser Glu Pro Pro Gly Phe Pro Thr Ser Gly Pro Arg Arg Pro Gly Cys Ser 415 410 Arg Lys Asn Arg Thr Arg Ser His Cys Arg Leu Gly Gln Ala Gly 425 430 Ser Gly Gly Gly Gly Thr Gly Asp Ser Glu Gly Ser Gly Ala Leu 440 445 Pro Ser Leu Thr Cys Ser Leu Thr Pro Leu Gly Leu Ala Leu Val 455 460 465 Leu Trp Thr Val Leu Gly Pro Cys 470 <210> 401 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 401 tggctgccct gcagtacctc tacc 24 <210> 402 <211> 24 <212> DNA

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<211> 798

<212> PRT

<213> Homo sapiens

<400> 405

Met Glu Ala Ser Gly Lys Leu Ile Cys Arg Gln Arg Gln Val Leu 1 5 10 15

Phe Ser Phe Leu Leu Gly Leu Ser Leu Ala Gly Ala Ala Glu 20 25 30

Pro Arg Ser Tyr Ser Val Val Glu Glu Thr Glu Gly Ser Ser Phe 35 40 45

Val Thr Asn Leu Ala Lys Asp Leu Gly Leu Glu Gln Arg Glu Phe
50 55 60

Ser Arg Arg Gly Val Arg Val Val Ser Arg Gly Asn Lys Leu His
65 70 75

Leu Gln Leu Asn Gln Glu Thr Ala Asp Leu Leu Leu Asn Glu Lys 80 85 90

Leu Asp Arg Glu Asp Leu Cys Gly His Thr Glu Pro Cys Val Leu 95 100 105

Arg Phe Gln Val Leu Leu Glu Ser Pro Phe Glu Phe Phe Gln Ala 110 115 120

Glu Leu Gln Val Ile Asp Ile Asn Asp His Ser Pro Val Phe Leu 125 130 135

Asp Lys Gln Met Leu Val Lys Val Ser Glu Ser Ser Pro Pro Gly
140 145 150

|                                       |   | Thr  | Thr | Phe | Pro | Leu<br>155  | Lys | Asn | Ala | Glu | Asp<br>160 | Leu | Asp | Val | Gly | G1n<br>165 |   |   |                    |                |
|---------------------------------------|---|------|-----|-----|-----|-------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|---|---|--------------------|----------------|
|                                       |   | Asn  | Asn | Ile | Glu | Asn<br>170  | Tyr | Ile | Ile | Ser | Pro<br>175 |     | Ser | Tyr | Phe | Arg<br>180 |   |   |                    |                |
|                                       |   | Val  | Leu | Thr | Arg | Lys<br>185  | Arg | Ser | Asp | Gly | Arg<br>190 | Lys | Tyr | Pro | Glu | Leu<br>195 |   |   | •                  |                |
|                                       |   | Val  | Leu | Asp | Lys | Ala<br>200  | Leu | Asp | Arg | Glu | Glu<br>205 | Glu | Ala | Glu |     | Arg<br>210 |   |   |                    |                |
|                                       |   | Leu  | Thr | Leu | Thr | Ala<br>215  | Leu | Asp | Gly | Gly | Ser<br>220 | Pro | Pro | Arg | Ser | Gly<br>225 |   |   | ,                  |                |
|                                       |   | Thr  | Ala | Gln |     | Tyr<br>-230 |     |     |     |     |            |     |     |     |     |            |   |   | <br>·- <del></del> | <del>-</del> · |
|                                       | • | Pro  | Glu | Phe | Glu | Gln<br>245  | Pro | Phe | Tyr | Arg | Val<br>250 | Gln | Ile | Ser | Glu | Asp<br>255 |   |   |                    |                |
|                                       |   | Ser  | Pro | Val | Gly | Phe<br>260  | Leu | Val | Val | Lys | Val<br>265 | Ser | Ala | Thr | Asp | Val<br>270 |   |   |                    |                |
|                                       |   | Asp  | Thr | Gly | Val | Asn<br>275  | Gly | Glu | Ile | Ser | Tyr<br>280 | Ser | Leu | Phe | Gln | Ala<br>285 |   |   |                    | ·              |
| • • •                                 |   | Ser  | Glu | Glu | Ile | Gly<br>290  | Lys | Thr | Phe | Lys | Ile<br>295 | Asn | Pro | Leu | Thr | Gly<br>300 |   | , |                    |                |
|                                       |   | ~Glu | Ile | Glu | Leu | Lys<br>305  | Lys | Gln | Leu | Asp | Phe<br>310 | Glu | Lys | Leu | Gln | Ser<br>315 |   | • |                    |                |
|                                       | * | Tyr  | Glu | Val | Asn | Ile<br>320  |     | Ala | Arg | Asp | Ala<br>325 | Gly | Thr | Phe | Ser | Gly<br>330 |   |   |                    |                |
| :                                     | : | Lys  | Cys | Thr | Val | Leu<br>335  | Ile | Gln | Val | Ile | Asp<br>340 | Val | Asn | Asp | His | Ala<br>345 |   | • |                    |                |
|                                       |   | Pro  | Glu | Val | Thr | Met<br>350  | Ser | Ala | Phe | Thr | Ser<br>355 |     | Ile | Pro | Glu | Asn<br>360 | • |   |                    |                |
|                                       |   | Ala  | Pro | Glu | Thr | Val<br>365  | Val | Ala | Leu | Phe | Ser<br>370 |     | Ser | Asp | Leu | Asp<br>375 | • |   |                    |                |
|                                       |   | Ser  | Gly | Glu | Asn | Gly<br>380  |     | Ile | Ser | Cys | Ser<br>385 |     | Gln | Glu | Asp | Leu<br>390 |   | · | ٠                  |                |
|                                       |   | Pro  | Phe | Leu | Leu | Lys<br>395  |     | Ala | Glu | Asn | Phe<br>400 |     | Thr | Leu | Leu | Thr<br>405 |   |   |                    |                |
|                                       |   | Glu  | Arg | Pro | Leu | Asp<br>410  |     | Glu | Ser | Arg | Ala<br>415 |     | Tyr | Asn | Ile | Thr<br>420 | • |   |                    |                |
| · · · · · · · · · · · · · · · · · · · |   | Ile  | Thr | Val | Thr | Asp<br>425  |     | Gly | Thr | Pro | Met<br>430 |     | Ile | Thr | Gln | Leu<br>435 |   |   |                    |                |

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| •                                       |          |     |       | ٠    |            |         | •      |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|---|----------|-----|-------|------|------------|---------|--------|-------|------------|--------------|------|-----------|------|-------|------------|---|-------|-----|-----|-----|-------|
|   |          |     |       |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   |          |     |       |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   |          |     |       |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   | Asn      | Met | Thr   | Val  | Leu        | Ile     | Ala    | Asp   | Val        | Asn          | Asp  | Asn       | Ala  | Pro   | Ala        |   |       | 4.  |     |     |       |
|   |          |     |       |      | 440        |         |        |       |            | 445          |      |           |      |       | 450        |   |       |     |     |     |       |
|   |          |     |       |      | _          | _       | m1     |       | <b>5</b> 1 | ** . 1       | D    | C1        | 7    | 7     |            |   |       |     |     |     |       |
|   | Phe      | Thr | Gln   | Thr  |            | Tyr     | Thr    | Leu   | Pne        | vai<br>460   | Arg  | GIU       | ASII | ASI   | 5er<br>465 |   | ٠.    |     |     |     |       |
|   | •        |     |       |      | 455        |         |        |       |            | 400          |      |           |      |       | 405        |   |       |     |     |     |       |
|   | Pro      | Ala | Leu   | His  | Tle        | Ara     | Ser    | Val   | Ser        | Ala          | Thr  | Asp       | Arg  | Asp   | Ser        | • |       |     |     |     | 2.00  |
|   |          |     |       |      | 470        |         |        |       |            | 475          |      |           |      |       | 480        |   |       |     |     |     |       |
|   |          |     | •     |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   | Gly      | Thr | Asn   | Ala  | Gln        | Val     | Thr    | Tyr   | Ser        |              | Leu  | Pro       | Pro  | Gln   |            |   |       |     |     |     |       |
| •                                       |          | •   |       |      | 485        | ,       |        |       |            | 490          |      |           |      | •     | 495        |   |       |     |     |     |       |
|   | 5        |     |       | D    | T          | n la sa | Com    | T     | . 37 - 3   | C~~          | т1 ^ | 7 an      | Λ1 a | 7 cn  | Acn        |   | . •   |     |     |     |       |
|   | Pro      | Hls | Leu   | Pro  | 500        | THE     | ser    | ьeu   | Val        | 505          | 116  | ASII      | мта  | Asp   | 510        |   |       |     |     |     | • • • |
|   | *: •     |     |       |      | 300        |         |        |       |            | 303          |      |           |      |       |            |   |       |     |     |     |       |
|   | Glv      | His | Leu   | Phe  | Ala        | Leu     | Arq    | Ser   | Leu        | Asp          | Tyr  | Glu       | Ala  | Leu   | Gln        |   |       |     |     |     | : .   |
| ·                                       |          |     |       |      | 515        |         |        |       |            | 520          |      |           |      |       | - 525      |   |       |     |     |     |       |
|   |          |     |       |      | :          | •       |        |       |            |              |      |           | ٠,   |       |            |   |       |     | ٠.  |     | ·     |
|   | Gly      | Phe | Gln   | Phe  |            | Val     | Gly    | Ala   | Ser        |              | His  | Gly       | Ser  |       |            |   |       |     | 4   | 2   |       |
|   |          |     |       |      | 530        |         |        |       |            | 535          | ,    |           | 1    |       | . 540      |   | •     |     |     |     |       |
|   | Lou      | Sor | Ser   | Glu  | Δ.<br>1 =  | T.e.11  | Vàl    | Δrα   | Val        | val          | Val  | Leu       | Asp  | Ala   | Asn        | , |       |     |     |     |       |
| ,                                       | Leu      | Ser | Ser   | GIU  | 545        | пси     | ٧٩٢    | 111.9 |            | 550          |      |           | p    |       | 555        |   |       | . , |     |     | , ,   |
|   |          | ٠.  | ٠.    |      |            |         |        |       | · .        | . •          |      |           |      |       |            |   |       |     |     |     |       |
|   | Asp      | Asn | Ser   | Pro  | Phe        | Val     | Leu    | Tyr   | Pro        | Leu          | Gln  | Asn       | Gly  | Ser   | Ala        |   | •     |     |     | 100 |       |
| • .                                     |          |     | A     | **   | 560        |         | ٠.     | ·     |            | 565          |      |           | •    |       | 5.70       |   |       |     |     |     |       |
|   |          |     | · ,   | 0.1  | + 37       |         | D      | 7     | 71.        | 71-          | C1   | Dwo       | C1   | П     | Tair       | • |       |     |     |     |       |
|   | Pro      | Cys | Thr   | Glu  | ьец<br>575 |         | PIO    | Arg   |            | 580          | GIU  | PIO       | GTA  | ıyı   | 585        |   |       |     |     |     | ·     |
| •                                       |          |     | ٠.    |      |            |         |        |       |            | . 500        |      |           |      |       |            |   |       |     |     |     | : .   |
|   | Val      | Thr | Lys   | Val  | Val        | Ala     | Val    | Asp   | Gly        | Asp          | Ser  | Gly       | Gln  | Asn   | Ala        |   |       | i   |     |     |       |
|   | •        |     | -     |      | 590        |         |        |       |            | 595          |      |           |      |       | 600        |   | : .   |     |     |     |       |
|   |          |     | ,     |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   | Trp      | Leu | Ser   | Tyr  |            |         | Leu    | Lys   | Ala        |              |      | Leu       | GLY  | Leu   |            |   |       | •   | . : |     |       |
|   |          |     |       |      | 605        |         | ٠.     |       |            | 610          |      |           |      |       | 615        |   | . ' ' |     |     |     |       |
|   | Glv      | Val | Trp   | Ala  | His        | Asn     | Glv    | Glu   | Val        | Ara          | Thr  | Ala       | Ara  | Leu   | Leu        |   |       |     |     |     |       |
|   | CII      | , , |       |      | 620        |         | 1      |       |            | 625          |      |           | _    |       | 630        |   |       |     |     |     |       |
|   |          |     |       |      |            | •       |        |       |            |              |      |           |      |       |            |   |       |     |     | ,   |       |
|   | Ser      | Glu | ( Arg | Asp  | Ala        | Ala     | Lys    | His   | Arg        |              |      | Val       | Leu  | Val   | Lys        |   |       | • • |     |     |       |
|   |          | r   |       |      | 635        |         | •      |       |            | 640          |      |           | 1.8  |       | 645        |   |       |     |     | ,   |       |
|   | <b>7</b> | 71  |       | . C1 | Dwa        | Dec     | 71 *** |       | 715        | Th.~         | רות. | Thr       | Len  | Hie   | Val        |   |       |     |     |     |       |
|   | Asp      | ASI | г сту | GIU  | 650        |         | ALG    | Ser   | . Ala      | 655          |      | . 1111    | Бей  |       | 660        | • |       |     |     |     |       |
|   |          |     |       |      |            |         |        | •     | •          |              | •    |           |      |       |            |   |       |     |     |     |       |
|   | Leu      | Let | ı Val | Asp  | Gly        | Phe     | Ser    | Gln   | Pro        | Tyr          | Leu  | Pro       | Leu  | Pro   | Glu        |   |       |     |     |     |       |
|   |          |     |       |      | 665        |         |        |       |            | 670          |      |           |      |       | 675        |   |       |     |     |     | 4     |
|   | ٠        |     |       |      | • •        | _       |        |       | _          | _            |      | <b></b> . |      |       |            |   | ٠.    |     |     |     | •     |
| 9                                       | Ala      | Ala | Pro   | Thr  |            |         | GLn    | Ala   | Asp        | ь Leu<br>685 |      | rnr       | vaı  | Tyr   | Leu<br>690 |   |       |     |     |     |       |
| * |          |     |       |      | 680        | ,       |        |       |            | 003          | ,    |           |      |       | . 050      | • |       |     |     |     | •     |
| •                                       | Val      | Val | Ala   | Leu  | Ala        | Ser     | Val    | Ser   | Ser        | Leu          | Phe  | Leu       | Phe  | Ser   | Val        |   |       |     | •   |     |       |
|   |          |     |       |      | 695        |         | ·.     |       |            | 700          |      |           |      |       | 705        |   |       |     |     |     |       |
|   |          |     | •     |      |            |         |        |       |            |              |      | ٠.        |      |       |            | • |       |     |     |     |       |
|   | Let      | Let | ı Phe | val  |            |         | . Arg  | Leu   | Cys        |              |      | Ser       | Arg  | , Ala | Ala        |   |       |     |     |     | •     |
|   |          |     |       | •    | 710        | )       |        |       |            | 715          | · .  |           | •    |       | 720        |   |       |     |     |     |       |
|   |          |     |       |      |            | •.      |        |       | )          |              |      |           |      |       |            |   | ٠,    |     |     |     |       |
|   |          |     |       |      |            |         | ı      |       |            |              |      | •         |      |       | •          |   |       |     |     |     |       |
|   |          |     |       |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |
|   |          |     | •     |      |            |         | •      |       |            |              |      |           | •    | - 10  |            |   |       |     |     |     |       |
|   |          |     |       |      |            |         |        |       |            |              |      |           | •    |       |            |   |       |     |     |     |       |
|   |          |     |       |      |            |         |        |       |            |              |      |           |      |       |            |   |       |     |     |     |       |

A Age

```
Ser Val Gly Arg Cys Leu Val Pro Glu Gly Pro Leu Pro Gly His
Leu Val Asp Met Ser Gly Thr Arg Thr Leu Ser Gln Ser Tyr Gln
Tyr Glu Val Cys Leu Ala Gly Gly Ser Gly Thr Asn Glu Phe Lys
Phe Leu Lys Pro Ile Ile Pro Asn Phe Pro Pro Gln Cys Pro Gly
Lys Glu Ile Gln Gly Asn Ser Thr Phe Pro Asn Asn Phe Gly Phe
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|                    | <211><212><213>   | PRI | ?     | nien | S          |     |     |     |      |            |      |       |      |     |            |
|--------------------|-------------------|-----|-------|------|------------|-----|-----|-----|------|------------|------|-------|------|-----|------------|
| <213> Homo sapiens |                   |     |       |      |            |     |     |     |      |            |      |       |      |     |            |
|                    | <400><br>Met<br>1 |     |       | Ala  | Ala<br>5   | Gly | Arg | Arg | Pro  | Pro<br>10  | Arg  | Val   | Met. | Arġ | Leu<br>15  |
|                    | Leu               | Gly | Trp   | Trp  | Gln<br>20  | Val | Leu | Leu | Trp  | Val<br>25  | Leu  | Gly   | Leu  | Pro | Val<br>30  |
|                    | Arg               | Gly | Val   | Glu  | Val<br>35  | Ala | Glu | Glu | Ser  | Gly<br>40  | Arg  | Leu   | Trp  | Ser | Glu<br>45  |
|                    | Glu               | Gln | Pro   | Ala  | His<br>50  | Pro | Leu | Gln | Val  | Gly<br>55  |      | Val   | Tyr  | Leu | Gly<br>60  |
|                    | Glu               | Glu | Glu   | Leu  | Leu<br>65  | His | Asp | Pro | Met  | Gly<br>70  | Gln  | Asp   | Arg  | Ala | Ala<br>75  |
|                    | Glu               | Glu | Ala   | Asn  | Ala<br>80  | Val | Leu | Gly | Leu  | Asp<br>85  | Thr  | Gln   | Gly  | Asp | His<br>90  |
|                    | Met               | Val | Met   | Leu  | Ser<br>95  | Val | Ile | Pro | Gly  | Glu<br>100 | Ala  | Glu   | Asp  | Lys | Val<br>105 |
|                    | Ser               | Ser | Glu   | Pro  | Ser<br>110 | Gly | Val | Thr | Cys  | Gly<br>115 | Ala  | Gly   | Gly  | Ala | Glu<br>120 |
|                    | Asp               | Ser | Arg   | Суѕ  | Asn<br>125 | Val | Arg | Glu | Ser  | Leu<br>130 | Phe  | Ser   | Leu  | Asp | Gly<br>135 |
|                    | Ala               | Gly | Ala   |      | Phe<br>140 |     | Asp | Arg | Glu  | Glu<br>145 | Glu  | Tyr   | Tyr  | Thr | Glu<br>150 |
|                    | Pro               | Glu | Val   | Ala  | Glu<br>155 | Ser | Asp | Ala | Ala  | Pro<br>160 | Thr  | Glu   | Asp  | Ser | Asn<br>165 |
|                    | Asņ               | Thr | Glu   | Ser  | Leu<br>170 |     | Ser | Pro | Lys  | Val<br>175 | Asn  | Cys   | Glu  | Gļu | Arg<br>180 |
|                    | Asn               | Ile | Thr   | _    | Leu<br>185 | Glu | Asn | Phe | Thr  | Leu<br>190 | Lys  | Ile   | Leu  | Asn | Met<br>195 |
|                    | Ser               | Gln | Asp   | Leu  | Met<br>200 |     | Phe | Leu | Asn  | Pro<br>205 | Asn  | Gly   | Ser  | Asp | Cys<br>210 |
|                    | Thr               | Leu | Val   | Leu  | Phe<br>215 | _   | Thr | Pro | Trp  | Cys<br>220 | Arg  | Phe   | Ser  | Ala | Ser<br>225 |
|                    | Leu               | Ala | Pro   | His  | Phe<br>230 |     | Ser | Leu | Pro  | Arg<br>235 | Ala  | Phe   | Pro  | Ala | Leu<br>240 |
|                    | His               | Phe | Leu   | Ala  | Leu<br>245 |     | Ala | Ser | Gln  | His<br>250 | Ser  | Ser   | Leu  | Ser | Thr<br>255 |
|                    | 7 ~~              | Dho | C1 ·· | Th ∽ | V-1        | מומ | W-1 | Dro | 7.~~ | Tla        | T ov | ī o:· | Dho  | Gln | Giv        |

Ala Lys Pro Met Ala Arg Phe Asn His Thr Asp Arg Thr Leu Glu 275 , 280 280 285

Thr Leu Lys Ile Phe Ile Phe Asn Gln Thr Gly Ile Glu Ala Lys 290 295 300

Lys Asn Val Val Thr Gln Ala Asp Gln Ile Gly Pro Leu Pro 305 310

Ser Thr Leu Ile Lys Ser Val Asp Trp Leu Leu Val Phe Ser Leu 320 325 330

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<sup>&</sup>lt;210> 415

<sup>&</sup>lt;211> 295

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;400> 415

| His | Cys | Cys | Leu | Gly<br>20  | Ser | Ala | Arg | Gly | Leu<br>25  | Phe | Leu | Phe              | Gly | Gln<br>30  |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|------------------|-----|------------|
| Pro | Asp | Phe | Ser | Tyr<br>35  | Lys | Arg | Ser | Asn | Cys<br>40  | Lys | Pro | Ile <sup>.</sup> | Pro | Val<br>45  |
| Asn | Leu | Gln | Leu | Cys<br>50  | His | Gly | Ile | Glu | Tyr<br>55  | Gln | Asn | Met              | Arg | Leu<br>60  |
| Pro | Asn | Leu | Leu | Gly<br>65  | His | Glu | Thr | Met | Lys<br>70  | Glu | Val | Leu              | Glu | Gln<br>75  |
| Ala | Gly | Ala | Trp | Ile<br>80  | Pro | Leu | Val | Met | Lys<br>85  | Gln | Cys | His              | Pro | Asp<br>90  |
| Thr | Lys | Lys | Phe | Leu<br>95  | Суѕ | Ser | Leu | Phe | Ala<br>100 | Pro | Val | Cys              | Leu | Asp<br>105 |
| Asp | Leu | Asp | Glu | Thr<br>110 | Ile | Gln | Pro | Cys | His<br>115 | Ser | Leu | Cys              | Val | Gln<br>120 |
| Val | Lys | Asp | Arg | Cys<br>125 | Ala | Pro | Val | Met | Ser<br>130 | Ala | Phe | Gly              | Phe | Pro<br>135 |
| Trp | Pro | Asp | Met | Leu<br>140 | Glu | Cys | Asp | Arg | Phe<br>145 | Pro | Gln | Asp              | Asn | Asp<br>150 |
| Leu | Cys | Ile | Pro | Leu<br>155 | Ala | Ser | Ser | Asp | His<br>160 | Leu | Leu | Pro              | Ala | Thr<br>165 |
| Glu | Glu | Ala | Pro | Lys<br>170 | Val | Cys | Glu | Ala | Cys<br>175 | Lys | Asn | Lys              | Asn | Asp<br>180 |
| Asp | Asp | Asn | Asp | Ile<br>185 | Met | Glu | Thr | Leu | Cys<br>190 | Lys | Asn | Åsp              | Phe | Ala<br>195 |
| Leu | Lys | Ile | Lys | Val<br>200 | Lys | Glu | Ile | Thr | Tyr<br>205 |     | Asn | Arg              | Asp | Thr<br>210 |
| Lys | Ile | Ile | Leu | Glu<br>215 | Thr | Lys | Ser | Lys | Thr<br>220 | Ile | Tyr | Lys              | Leu | Asn<br>225 |
| Gly | Val | Ser | Glu | Arg<br>230 |     | Leu | Lys | Lys | Ser<br>235 | Val | Leu | Trp              | Leu | Lys<br>240 |
| Asp | Ser | Leu | Gln | Cys<br>245 |     | Cys | Glu | Glu | Met<br>250 |     | Asp | Ile              | Asn | Ala<br>255 |
| Pro | Tyr | Leu | Val | Met<br>260 |     | Gln | Lys | Gln | Gly<br>265 |     | Glu | Leu              | Val | Ile<br>270 |
| Thr | Ser | Val | Lys | Arg<br>275 |     | Gln | Lys | Gly | Gln<br>280 |     | Glu | Phe              | Lys | Arg<br>285 |
| Ile | Ser | Arg | Ser | Ile        | Arg | Lys | Leu | Gln | Cys        |     |     |                  |     |            |

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|     |     |     |          |     |            |     |       |      |     |            |      |       |       |       |            | 1 |   |     |      |                   |
|     | Leu | Gly | Gly<br>、 | Met | Ile<br>260 | Gly | Ile   | Ser  | Ala | Ser<br>265 | Phe  | Ser   | Ala   | Leu   | Leu<br>270 |   |   |     |      |                   |
| . • | Glu | Gln | Ile      | Leu | Cys<br>275 | Ala | Ser   | Gly  | His | Ser<br>280 | Ser  | Gly   | Phe   | Ser   | Gly<br>285 |   | • |     |      |                   |
|     | Leu | Cys | Gly      | Ala | Leu<br>290 |     | Ile   | Thr  | Phe | Gly<br>295 | Ile  | Leu   | Gly   | Ala   | Leu ·      |   |   |     |      |                   |
|     | Ala | Leu | Gly      | Pro | Tyr<br>305 | Val | Asp   | Arg  | Thr | Lys<br>310 | His  | Phe   | Thr   | Glu   | Ala<br>315 |   |   |     |      |                   |
|     | Thr | Lys | Ile      | Gly | Leu<br>320 | Cys | Leu   | Phe  | Ser | Leu<br>325 | Ala  | Cys   | Val   | Pro   | Phe<br>330 |   |   |     |      | :                 |
|     | Ala | Leu | Val      | Ser | Gln<br>335 | Leu | -Gln- | Gly  | Gln | Thr<br>340 | -Leu | -Ala- | -Leu  | -Ala  | Ala -      |   |   | ( - | <br> | <br>. <del></del> |
|     | Thr | Cys | Ser      | Leu | Leu<br>350 | Gly | . Leu | Phe  | Gly | Phe<br>355 | Ser  | Val   | Gly   | Pro   | Val<br>360 |   |   |     |      | . *               |
|     | Ala | Met | Glu      | Leu | Ala<br>365 | Val | Glu   | Cys  | Ser | Phe<br>370 | Pro  | Val   | Gly   | Glu   | Gly<br>375 |   |   |     |      |                   |
|     | Ala | Ala | Thr      | Gly | Met<br>380 | Ile | Phe   | ,Val | Leu | Gly<br>385 | Gln  | Ala   | Glu   | Gly   | Ile<br>390 |   |   |     |      | ,38 s             |
| a a | Leu | Ile | Met      | Leu | Ala<br>395 | Met | Thr   | Ala  | Leu | Thr<br>400 | Val  | Arg   | Arg   | Ser   | Glu<br>405 |   |   | •   |      |                   |
|     | Pro | Ser | Leu      | Ser | Thr<br>410 | Cys | Gln   | Gln  | Gly | Glu<br>415 | Asp  | Pro   | Leu   | Asp   | Trp<br>420 |   |   |     |      |                   |
|     | Thr | Val | Ser      | Leu | Leu<br>425 | Leu | Met   | Ala  | Gly | Leu<br>430 | Cys  | Thr   | Phe   | Phe   | Ser<br>435 |   |   |     |      | •                 |
|     | Cys | Ile | Leu      | Ala | Val<br>440 | Phe | Phe   | His  | Thr | Pro<br>445 | _    | Arg   | Arg   | Leu   | Gln<br>450 |   |   |     |      |                   |
|     | Ala | Glu | Ser      | Gly | Glu<br>455 |     | Pro   | Ser  | Thr | Arg<br>460 |      | Ala   | Val   | Gly   | Gly<br>465 |   |   |     |      |                   |
|     | Ala | Asp | Ser      | Gly | Pro<br>470 | Gly | Val   | Asp  | Arg | Gly<br>475 |      | Ala   | Gly   | Arg   | Ala<br>480 |   |   |     |      |                   |
| ٠   | Gly | Val | Leu      | Gly | Pro<br>485 |     | Thr   | Ala  | Thr | Pro<br>490 |      | Cys   | Thr   | Ala   | Arg<br>495 |   |   |     |      |                   |
|     | Gly | Ala | Ser      | Leu | Glu<br>500 |     | Pro   | Arg  | Gly | Pro<br>505 |      | Ser   | Pro   | His   | Pro<br>510 |   |   |     |      |                   |
|     | Ala | Cys | His      | Arg | Ala<br>515 |     | Pro   | Arg  | Ala | Gln<br>520 |      | Pro   | Ala   | ·Ala  | Thr<br>525 |   |   |     |      |                   |
|     | Asp | Ala | Pro      | Ser | Arg<br>530 |     | Gly   | Arg  | Leu | Ala<br>535 |      | , Arg | y Val | . Gln | Ala<br>540 |   |   |     |      |                   |

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## <400> 425

Met Met Gln Leu Leu Gln Leu Leu Gly Leu Leu Gly Pro Gly
1 5 10 15

<sup>&</sup>lt;210> 425

<sup>&</sup>lt;211> 1184

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|    |         |     |     |     |             |     |     |     |          |            |     |     |       |     |             |   | • |   |   | •   |     |
|----|---------|-----|-----|-----|-------------|-----|-----|-----|----------|------------|-----|-----|-------|-----|-------------|---|---|---|---|-----|-----|
|    | Gly     | Tyr | Leu | Phe | Leu<br>20   | Leu | Gly | Asp | Cys      | Gln<br>25  | Glu | Val | Thr   | Thr | Leu<br>30   |   |   |   |   |     |     |
|    | Thr     | Val | Lys | Tyr | Gln<br>35   | Val | Ser | Glu | Glu      | Val<br>40  | Pro | Ser | Gly   | Thr | Val<br>45   |   |   |   |   |     |     |
|    | Ile     | Gly | Lys | Leu | Ser<br>50   | Gln | Glu | Leu | Gly      | Arg<br>55  | Glu | Glu | Arg   | Arg | Arg<br>60   |   |   |   |   |     |     |
|    | Gln     | Ala | Gly | Ala | Ala<br>65   | Phe | Gln | Val | Leu<br>, | Gln<br>70  | Leu | Pro | Gln   | Ala | Leu<br>75   |   |   |   |   | . , |     |
|    | Pro     | Ile | Gln | Val | Asp<br>80   | Ser | Glu | Glu | Gly      | Leu<br>85  | Leu | Ser | Thr   | Gly | Arg<br>90   |   |   |   | • |     | . 7 |
|    | <br>Arg | Leu | Asp | Arg | Glu<br>- 95 | Gln | Leu | Cys | Arg      | Gln<br>100 |     | Asp | Pro   | Cys | Leu_<br>105 |   |   |   |   |     |     |
|    | Val     | Ser | Phe | Asp | Val<br>110  | Leu | Ala | Thr | Gly      | Asp<br>115 | Leu | Ala | Leu   | Ile | His<br>120  |   |   | • | • |     |     |
|    | Val     | Glu | Ile | Gln | Val         | Leu | Asp | Ile | Asn      | Asp<br>130 |     | Gln | Pro   | Arg | Phe<br>135  |   |   |   |   |     |     |
|    | Pro     | Lys | Gly | Glu | Gln<br>140  | Glu | Leu | Glu | Ile      | Ser<br>145 |     | Ser | Ala   | Ser | Leu<br>150  | • |   |   |   |     | *   |
|    | Arg     | Thr | Arg | Ile | Pro<br>155  | Leu | Asp | Arg | Ala      | Leu<br>160 |     | Pro | Asp   | Thr | Gly<br>165  |   |   |   |   |     |     |
|    | Pro     | Asn | Thr | Leu |             | Thr | Tyr | Thr | Leu      | Ser<br>175 |     | Ser | Glu   | His | Phe         |   |   |   |   |     |     |
|    | Ala     | Leu | Asp | Val |             | Val | Gly | Pro | Asp      |            | Thr | Lys | His   | Ala | Glu<br>195  |   |   |   |   |     |     |
|    | Leu     | Ile | Val | Val |             | Glu | Leu | Asp | Arg      |            | Ile | His | Ser   | Phe |             | • |   |   | , |     |     |
|    | Asp     | Leu | Val | Leu |             |     | Tyr | Asp | Asn      |            | Asn | Pro | Pro   | Lys | Ser<br>225  |   |   |   |   |     | •   |
|    | Gly     | Thr | Ser | Leu | Val         | Lys | Val | Asn | Val      | Leu        | Asp | Ser | Asn   | Asp | Asn<br>240  |   |   |   |   |     |     |
| •  | Ser     | Pro | Ala | Phe |             | Glu | Ser | Ser | Leu      |            | Leu | Glu | Ile   | Gln | Glu         |   |   |   |   |     |     |
| ·  | Asp     | Ala | Ala | Pro |             | Thr | Leu | Leu | ı Ile    |            | Lev | Thr | Ala   | Thr | 255<br>Asp  |   |   | • |   |     |     |
|    | Pro     | Asp | Gln | Gly | 260<br>Pro  |     | Gly | Glu | ı Val    | 265<br>Glu |     | Phe | . Leu | Ser | 270<br>Lys  |   |   |   |   | •   |     |
| ., |         |     |     |     | 275         |     |     |     |          | 280        | )   |     |       |     | 285<br>Lys  |   |   | ٠ | ٠ |     |     |
|    |         |     |     |     | 290         |     |     | - F |          | 295        |     |     |       |     | 300         |   |   |   |   |     | ,   |
|    |         |     |     |     |             |     |     |     |          |            |     |     |       |     |             |   |   |   |   |     |     |

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|     |     |     |     |             |          |      | ,   |     |            |     |     |     |     |            |    |
|-----|-----|-----|-----|-------------|----------|------|-----|-----|------------|-----|-----|-----|-----|------------|----|
| Thr | Gly | Gln | Val | Ile<br>305  | Leu      | Arg  | Arg | Pro | Leu<br>310 | Asp | Tyr | Glu | Lys | Asn<br>315 |    |
| Pro | Ala | Tyr | Glu | Val<br>320  | Asp      | Val  | Gln | Ala | Arg<br>325 | Asp | Leu | Gly | Pro | Asn<br>330 |    |
| Pro | Ile | Pro | Ala | His<br>335  | Cys<br>, | Lys  | Val | Leu | Ile<br>340 | Lys | Val | Leu | Asp | Val<br>345 |    |
| Asn | Asp | Asn | Ile | Pro<br>350  | Ser      | Ile  | His | Val | Thr<br>355 | Trp | Ala | Ser | Gln | Pro<br>360 |    |
| Ser | Leų | Val |     | Glu<br>365  | Ala      | Leu  | Pro | Lys | Asp<br>370 | Ser | Phe | Ile | Ala | Leu<br>375 | 1  |
| Val | Met | Ala | Asp | Asp<br>380  | Leu      | Asp  | Ser | Gly | His<br>385 | Asn | Gly | Leu | Val | His<br>390 |    |
| Cys | Trp | Leu | Ser | Gln<br>395  | Glu      | Leu  | Gly |     | Phe<br>400 | Arg | Leu | Lys | Arg | Thr<br>405 |    |
| Asn | Gly | Asn | Thr | Tyr<br>410  | Met      | Leu  | Leu | Thr | Asn<br>415 | Ala | Thr | Leu | Asp | Arg<br>420 |    |
| Glu | Gln | Trp |     | Lys<br>.425 | Tyr      | Thr  | Leu | Thr | Leu<br>430 | Leu | Ala | Gln | Asp | Gln<br>435 |    |
| Gly | Leu | Gln | Pro | Leu<br>440  |          | Ala  | Lys | Lys | Gln<br>445 | Leu | Ser | Ile | Gln | Ile<br>450 |    |
| Ser | Asp | Ile | Asn | Asp<br>455  | Asn      | Ala  | Prő | Val | Phe<br>460 | Glu | Lys | Ser | Arg | Tyr<br>465 | ,  |
| Glu | Val | Ser | Thr | Arg<br>470  | Ġlu      | Asn  | Asn | Leu | Pro<br>475 | Ser | Leu | His | Leu | Ile<br>480 | •. |
| Thr | Ile | Lys | Ala | His<br>485  | Asp      | Ala  | Asp | Leu | Gly<br>490 |     | Asn | Gly | Lys | Val<br>495 |    |
| Ser | Tyr | Arg | Ile | Gln<br>500  | Asp      | Ser  | Pro | Val | Ala<br>505 |     | Leu | Val | Ala | Ile<br>510 |    |
| Asp | Ser | Asn | Thr | Gly<br>515  | Glu      | Val  | Thr | Ala | Gln<br>520 |     | Ser | Leu | Asn | Tyr<br>525 |    |
| Glu | Glu | Met | Ala | Gly<br>530  | Phe      | ·Glu | Phe | Gln | Val<br>535 |     | Ala | Glu | Asp | Ser<br>540 |    |
| Gly | Gln | Pro | Met | Leu<br>545  | Aļa      | Ser  | Ser | Val | Ser<br>550 |     | Trp | Val | Ser | Leu<br>555 |    |
| Leu | Asp | Ala | Asn | Asp<br>560  | Asn      | Ala  | Pro | Glu | Val<br>565 |     | Gln | Pro | Val | Leu<br>570 |    |
| Ser | Asp | Gly | Lys | Ala<br>575  |          | Leu  | Ser | Val | Leu<br>580 |     | Asn | Ala | Ser | Thr<br>585 |    |
|     |     |     |     |             |          |      |     |     |            |     |     |     |     |            |    |

|     |            |     |     |     |            | •   |     |       |       |             |     |              |          |      |            |
|-----|------------|-----|-----|-----|------------|-----|-----|-------|-------|-------------|-----|--------------|----------|------|------------|
|     | Gly        | His | Leu | Leu | Val<br>590 | Pro | Ile | Glu   | Thr   | Pro.<br>595 | Asn | Gly          | Leu      | Gly  | Pro<br>600 |
|     | Ala        | Gly | Thr | Asp | Thr<br>605 | Pro | Pro | Leu   | Ala   | Thr<br>610  | Ḥis | Ser          | Ser<br>: | Arg  | Pro<br>615 |
| •   | Phe        | Leu | Leu | Thr | Thr<br>620 | Ile | Val | Ala   | Arg   | Asp<br>625  | Ala | Asp          | Ser      | Gly  | Ala<br>630 |
|     | Asn        | Gly | Glu | Pro | Leu<br>635 | Tyr | Ser | Ile   | Arg   | Asn<br>640  | Gly | Asn          | Glu      | Ala  | His<br>645 |
|     | Leu        | Phe | Ile | Leu | Asn<br>650 | Pro | His | Thr   | Gly   | Gln<br>655  | Leu | Phe          | Val      | Asn  | Val<br>660 |
|     | <u>Thr</u> | Asn | Ala | Ser | Ser<br>665 | Leu | Ile | Gly   | Ser   | Glu<br>670  | Trp | Glu          | Leu      | Glu  | Ile<br>675 |
| . • | Val        | Val | Glu | Asp | Gln<br>680 | Gly | Ser | Pro   | .Pro  | Leu<br>685  | Gln | Thr          | Arg      | Ala  | Leu<br>690 |
|     |            |     |     |     | 695        | Val |     |       |       | 700         |     |              |          |      | 705        |
|     |            | -   |     |     | 710        | Ala |     |       |       | 715         |     |              |          |      | 720        |
| *   | •          |     |     |     | 725        | Leu |     |       |       | 730         |     |              | •        |      | 735        |
| 000 |            |     |     |     | 740        | Arg |     |       |       | 745         |     |              |          |      | 750        |
|     |            |     |     |     | 755        | Glu |     |       |       | 760         |     |              |          |      | 765        |
|     | Pro        |     |     |     | 770        | •   |     |       |       | 775         |     |              |          |      | 780        |
|     |            |     |     |     | 785        |     |     | ,     |       | 790         |     |              |          |      | His<br>795 |
|     | :          |     |     |     | 800        | Glu |     |       |       | 805         |     |              |          |      | 810        |
|     |            |     |     |     | 815        | Phe |     |       |       | 820         | •   |              |          |      | 825        |
|     |            |     |     |     | 830        |     |     |       |       | 835         |     |              |          |      | Glu<br>840 |
| *   | ,          |     |     |     | 845        |     |     |       |       | 850         |     |              |          |      | Gln<br>855 |
|     | Arg        | Asn | Ala | ser | Arg<br>860 |     | ASN | . Leu | . Asn | 865         |     | o GIU        | rro      | GIII | Pro<br>870 |
|     |            | •   |     |     |            |     |     |       |       |             |     |              |          |      |            |
|     |            | ÷   |     |     |            |     |     |       |       |             |     | ~~~ <b>-</b> |          | _    |            |

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|---|---------|---------------------|----------|-----------|--------------------|-----------|---------------|------------|--------|
|   |         |                     |          |           |                    |           |               |            |        |
|   |         | ·                   |          |           |                    |           |               |            |        |
|   | Ala Thr | Gly Gln Pro         |          |           | eu Lys Val<br>80   | Ala Gly   | Ser<br>885    |            |        |
|   | Pro Thr | Gly Arg Leu         | Ala Gly  | Asp Gln G | ly Ser Glu         | Glu Ala   | Pro .         | 4.         |        |
|   | Gln Arg | Pro Pro Ala         | Ser Ser  | Ala Thr L |                    | Gln Arg   |               |            |        |
|   | Leu Asn | 905<br>Gly Lys Val  |          | Glu Lys G |                    | Pro Arg   | 915<br>Gln    |            |        |
|   | Ile Leu | 920<br>Arg Ser Leu  |          |           | 025<br>Mal Ala Ala | ,         | 930<br>Glu    |            | ;<br>; |
|   |         | 935<br>Pro Val Glu  |          | 9         | 040                | •         | 945           |            |        |
| , | = F., v | 950<br>Ser Gln Leu  |          | 9         | 955                |           | 960           |            |        |
|   |         | 965<br>Pro Asn His  | •        | · g       |                    |           | 975           |            | =      |
|   |         | 980                 |          | 9         | 985                |           | 990           |            | »      |
| Y | ٠.      | Arg Ser Ala         | ;        | . 10      | 000                |           | 1005          |            | *      |
|   |         | Gly Gln Thi         | )        | 10        | 015                |           | 1020          |            |        |
|   |         | Glu Asp Let<br>102  | <b>.</b> | . 10      | 030                | 4         | 1035          |            |        |
|   | Ser Ser | Leu Leu Asp<br>1040 |          |           | Leu Ala Lei<br>045 |           | Leu<br>1050   | <i>i</i> . |        |
|   | Ser Ala | Pro Asp Pro<br>105  |          |           | Arg Leu Sei<br>060 |           | Leu<br>1065   | 1          |        |
| · | Thr Thr | Asn Tyr Arc         |          |           | Ser Pro Asp<br>075 | o Ala Ala | Ala<br>1080   | •          |        |
|   | Thr Glu | Glu Pro Arc<br>108  |          |           | Phe Gly Ly:<br>090 |           | Ala<br>1095   | ٠.         |        |
|   | Pro Glu | Leu Ser Pro         |          | _         | Leu Ala Se<br>105  |           | Val<br>1110   |            | . •    |
| • | Ser`Glu | Met Ser Se<br>111   |          |           | Leu Leu Gl<br>120  | u Gln Arg | Ser<br>1125   |            |        |
| • | Ser Met | Pro Val Gl          |          |           | Ala Leu Aro<br>135 | g Arg Leu | 1 Ser<br>1140 |            |        |
|   | Val Cys | Gly Arg Th          |          |           | Leu Ala Th         | r Ser Ala | Ala<br>1155   |            |        |
|   | ٠       |                     |          |           |                    | ·         |               |            |        |
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|   |         |                     |          |           | _                  |           |               |            |        |

Ser Gly Met Lys Val Gln Gly Asp Pro Gly Gly Lys Thr Gly Thr 1160 1165 Glu Gly Lys Ser Arg Gly Ser Ser Ser Ser Ser Arg Cys Leu ,1175 1180 <210> 426 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 426 gtaagcacat gcctccagag gtgc 24 <210> 427 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 427 gtgacgtgga tgcttgggat gttg 24 <210> 428 <211> 50 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe . <400> 428 tggacacctt cagtattgat gccaagacag gccaggtcat tctgcgtcga 50 <210> 429 <211> 2037 <212> DNA <213> Homo sapiens <400> 429 eggacgegtg ggeggacgeg tgggggagag cegeagteec ggetgeagea 50 / cctgggagaa ggcagaccgt gtgagggggc ctgtggcccc agcgtgctgt 100 ggcctcgggg agtgggaagt ggaggcagga gccttcctta cacttcgcca 150

tgagtttcct catcgactcc agcatcatga ttacctccca gatactattt 200

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175

Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg Leu Leu Gln

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| Gly | Phe   | Trp | Gly   | Met<br>230 | Ile | Lys | Ser   | Val | Thr<br>235 | Thr | Ser   | Ala   | Ser | Gly<br>240 |
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| Phe | Asn   | Phe | Leů   | Gly<br>290 | Tyr | Phe | Phe   | Ser | Ile<br>295 | Tyr | Cys   | Val   | Trp | Lys<br>300 |
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| Gly | Ile   | Gln | Phe   | Asp<br>335 | Val | Lys | Phe   | Trp | Ser<br>340 | Gln | His   | Ile   | Ser | Phe<br>345 |
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| Ser | Asn   | Val | Ile   | Val<br>380 |     | Leu | Leu   | Ala | Gln<br>385 |     | Met   | Gly   | Met | Tyr<br>390 |
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| Lys | s Gln | Met | : Ala | Pro<br>455 |     |     |       |     | ¥ .        |     |       |       |     |            |
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65 70 75

Gln Ala Leu Ala Leu Pro Gly Gln Gln Ala Asn Arg Thr Gly Gly
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Leu Phe Ala Cys Pro Leu Ser Leu Glu Glu Thr Asp Cys Tyr Arg

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|          |      |       | •     |       | 125   |     | ٠     |       | _     | 130   |     | _     |       | _     | 135   |   |   |   |   |   |       |
|          | Lvs  | Ile   | Val   | Thr   | Cys   | Ala | His   | Arg   | Tyr   | Glu   | Ala | Arg   | Gln   | Arg   | Val   |   |   |   |   |   |       |
|          | •    |       |       |       | 140   |     |       |       | _     | 145,  |     | *     |       | _     | 150   |   |   |   |   |   |       |
|          | Asp  | Gln   | Ile   | Leu   | Glu   | Thr | Arg   | Asp   | Met   | Ile   | Gly | Arg   | Cys   | Phe   | Val   |   |   |   |   |   |       |
|          | •    |       |       |       | 155   |     | Ī     | •     | . '-  | 160   | _   | •     | •     |       | 165   |   |   |   |   | ; | •     |
|          | Leu  | Ser   | Gln   | Asp   | Leu   | Ala | Ile   | Arg   | Asp   | Glu   | Leu | Asp   | Gly   | Gly   | Glu   |   |   |   |   | • |       |
|          |      |       |       | •     | 170   |     |       | -     | -     | 175   |     | _     | _     | _     | 180   |   |   |   |   |   | ·     |
|          | Trp  | Lvs   | Phe   | Ċvs   | Glu   | Gly | Arg   | Pro   | Gln   | Gly   | His | Glu   | Gln   | Phe   | Gly   |   |   |   |   |   |       |
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|          | ,    |       |       |       | 200   |     | i     |       |       | 205   |     |       | •     |       | 210   |   |   |   |   |   | •     |
|          | Tvr  | Leu   | Leu   | Phe   | Gly   | Ala | Pro   | Gly   | Thr   | Tyr   | Asn | Trp   | Lys   | Gly   | Thr   |   |   |   |   |   |       |
| •••      |      |       |       |       | 215   |     |       | ·     |       | 220   |     | Ī     | _     | _     | 225   |   |   |   | • |   | ,     |
|          | Ala  | Ara   | Val   | Glu   | Leu   | Cys | Ala   | Gln   | Gly   | Ser   | Ala | Asp   | Leu   | Ala   | His   |   |   |   |   |   | y.    |
|          |      |       |       |       | 230   | •   |       |       | _     | 235   |     |       |       |       | 240   |   |   |   |   |   |       |
|          | Leu  | Asp   | Asp   | Gly   | Pro   | Tyr | Glu   | Ala   | Gly   | Gly   | Glu | Lys   | Glu   | Gln   | Asp   | • |   |   |   |   |       |
|          |      | •     | -     |       | 245   | _   |       | •     |       | 250   |     |       |       |       | 255   |   |   |   |   |   |       |
| •        | Pro  | Arg   | Leu   | Ile   | Pro   | Val | Pro   | Ala   | Asn   | Ser   | Tyr | Phe   | Gly   | Phe   | Ser   |   |   |   |   | • |       |
| •        |      | ,     |       |       | 260   |     | ,     |       |       | 265   |     |       |       |       | 270   |   |   |   |   |   |       |
|          | ·Ile | Asp   | Ser   | Gly   | Lys   | Gly | Leu   | Val   | . Arg | Ala   | Glu | Glu   | Leu   | Ser   | Phe   |   |   |   |   |   |       |
|          | ٠    | •     |       | ·     | 275   |     |       |       |       | 280   |     |       |       |       | 285   |   |   |   |   |   |       |
|          | Val  | Ala   | Glv   | Ala   | Pro   | Arq | Ala   | Asn   | . His | Lys   | Gly | Ala   | Val   | . Val | lle   |   |   |   |   |   |       |
|          |      |       |       |       | 290   | _   |       |       |       | 295   |     |       |       |       | 300   |   |   | • |   |   |       |
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|          | Val  | Tvr   | Leu   | ı Asr | ı Gln | Glv | , Gly | / His | s Trp | Àla   | Gly | , Ile | Sei   | r Pro | o Leu |   |   |   |   |   |       |
|          |      | - 1,  |       |       | 365   |     |       |       | -     | 370   |     | •     |       |       | 375   |   |   |   |   |   |       |
|          | Aro  | r Lei | ı Cvs | s Glv | / Ser | Pro | Asr   | Se    | r Met | : Phe | Gly | , Ile | e Sei | r Le  | u Ala |   |   |   |   |   |       |
|          | 5    |       | 4 -   |       | 380   |     | •     |       |       | 385   |     |       |       |       | 390   |   |   |   |   |   |       |
|          |      |       |       |       |       |     |       |       |       |       |     |       |       |       |       |   |   |   |   |   |       |
|          |      |       |       |       |       |     |       |       |       |       |     |       |       |       |       |   |   |   |   |   |       |
|          |      |       | •     |       |       |     |       |       |       |       |     |       |       |       |       |   |   |   |   |   | **    |
| IL<br>IS |      |       |       |       |       |     |       |       |       |       |     |       |       |       |       |   |   |   |   |   | • • • |
| 1/4      |      |       |       |       |       |     |       |       |       |       |     |       |       |       |       |   |   |   |   |   |       |

| Val | Leu   | Gly   | Asp   | 395        | Asn | GIN | Asp      | етх | 400.                |     | ASP | TTE | Ala  | 405                     |   |      |          |     |       |   |            |
|-----|-------|-------|-------|------------|-----|-----|----------|-----|---------------------|-----|-----|-----|------|-------------------------|---|------|----------|-----|-------|---|------------|
| Gly | Ala   | Pro   | Phe   | Asp<br>410 | Gly | Asp | Gly      | Lys | Val<br>415          | Phe | Ile | Tyr | His  | Gly<br>420              |   |      |          |     |       |   |            |
| Sea | Ser   | Leu   | Gly   | Val<br>425 | Val | Ala | Lys<br>· | Pro | Ser<br>430          | Gln | Val | Leu | Glu  | Gly<br>435              |   |      |          |     |       |   |            |
| Glı | a Ala | Val   | Gly   | Ile<br>440 | Lys | Ser | Phe      | Gly | Tyr<br>445          | Ser | Leu | Ser | Gly  | Ser<br>450              |   |      |          |     |       |   | •          |
| Le  | a Asp | Met   | Asp   | Gly<br>455 | Asn | Gln | Tyr      | Pro | Asp<br>460          | Leu | Leu | Val | ·Gly | Ser<br>465              |   |      |          |     |       |   | •          |
| Le  | ı Ala | Asp   | Thr   | Ala<br>470 | Val | Leu | Phe      | Arg | Ala<br>4 <u>7</u> 5 |     | Pro | Ile | Leu  | His<br>480_             |   | <br> |          |     | سـ سـ |   | . ·<br>. — |
| Va. | l Ser | His   | Glu   | Val<br>485 | Ser | Ile | Ala      | Pro | Arg<br>490          | Ser | Ile | Asp | Leu  | Glu<br>495              |   |      |          |     |       | • |            |
| Gl  | n Pro | Asn   | Cys   | Ala<br>500 | Gly | Gly | His      | Ser | Val<br>505          | Cys | Val | Asp | Leu  | Arg<br>510              |   |      |          |     |       |   |            |
| Va  | l Cys | Phe   | Ser   | Tyr<br>515 | Ile | Ala | Val      | Pro | Ser<br>520          | Ser | Tyr | Ser | Pro  | Thr<br>525              |   |      |          | • • | •     |   |            |
| Va  | l Ala | Leu   | Asp   | Tyr<br>530 | Val | Leu | Asp      | Ala | Asp<br>535          | Thr | Asp | Arg | Arg  | Leu<br>540              |   |      |          |     |       |   |            |
| Ar  | g Gly | Gln   | Val   | Pro<br>545 | Arg | Val | Thr      | Phe | Leu<br>550          | Ser | Arg | Aśn | Leu  | Glu<br>555              |   |      |          |     |       |   | J.         |
| Gl  | u Pro | Lys   | His   | Gln<br>560 | Ala | Ser | Gly      | Thr | Val<br>565          | Trp | Leu | Lys | His  | Gln<br>570              | • |      |          |     |       |   |            |
| Hi  | s Asp | Arg   | Val   | Cys<br>575 |     | Asp | Ala      | Met | Phe<br>580          |     | Leu | Gln | Glu  | 1 Asn<br>585            |   |      |          |     |       |   | · · ·      |
| Va  | l Lys | Asp   | Lys   | Leu<br>590 |     | Ala | Ile      | Val | Val<br>595          |     | Leu | Ser | Tyr  | Ser<br>600              |   | . ;  |          |     |       |   |            |
| Le  | u Gln | Thr   | Pro   | Arg<br>605 |     | Arg | Arg      | Gln | Ala<br>610          |     | Gly | Gln | Gly  | Leu<br>615              | • |      |          |     |       |   |            |
| Pr  | o Pro | Val   | . Ala | Pro<br>620 |     | Leu | Asn      | Ala | His<br>625          |     | Pro | Ser | Thr  | Gln<br>630              |   |      |          |     |       |   |            |
| Ar  | g Ala | Glu   | Ile   | His<br>635 |     | Leu | Lys      | Gln | Gly<br>640          |     | Gly | Glu | Asp  | Lys<br>645 <sub>.</sub> |   |      |          |     |       |   |            |
| 11  | e Cys | Gln   | Ser   | 650        |     | Gln | Leu      | Val | His<br>655          |     | Arg | Phe | cys  | 660                     | • |      | <i>:</i> |     |       |   |            |
| Ar  | g Val | . Ser | Asp   | Thr<br>665 |     |     | Gln      |     | Leu<br>670          |     | Met | Asp | Val  | 675                     |   |      |          |     |       |   |            |
|     |       |       |       |            |     |     |          |     |                     |     |     |     |      |                         |   |      |          |     |       |   |            |

₹ 22

|        |         |     |     |     |              |     |     |     |     |            |     |     |          |       |            |     |   |   | ·  |                          |   |
|--------|---------|-----|-----|-----|--------------|-----|-----|-----|-----|------------|-----|-----|----------|-------|------------|-----|---|---|----|--------------------------|---|
|        | Gly     | Thr | Thr | Ala | Leu<br>680   | Phe | Ala | Leu | Ser | Gly<br>685 |     | Pro | Val      | Ile   | Gly<br>690 |     |   | • |    |                          |   |
|        | Leu     | Glu | Leu | Met | Val<br>695   | Thr | Asn | Leu | Pro | Ser<br>700 |     | Pro | Ala      | Gln   | Pro<br>705 |     |   |   |    |                          |   |
|        | Gln     | Ala | Asp | Gly | Asp<br>710   | Asp | Ala | His | Glu | Ala<br>715 | Gln | Leu | Leu      | Val   | Met<br>720 |     |   |   |    |                          |   |
| ,      | Leu     | Pro | Asp | Ser | Leu<br>725   | His | Tyr | Ser | Gly | Val<br>730 | Arg | Ala | Leu      | Asp   | Pro<br>735 |     |   |   |    |                          |   |
|        | Ala     | Glu | Lys | Pro | Leu<br>740   | Cys | Leu | Ser | Asn | Glu<br>745 | Asn | Ala | Ser      | His   | Val<br>750 |     |   |   |    |                          |   |
|        | Glu<br> | Cys | Glu |     | Gly<br>-755- |     |     |     |     |            |     |     |          |       |            |     |   |   |    | n name of states and are | - |
|        | Phe     | Tyr | Leu | Ile | Leu<br>770   | Ser | Thr | Ser | Gly | Ile<br>775 | Ser | Ile | :<br>Glu | Thr   | Thr<br>780 |     |   |   |    |                          |   |
|        | Glu     | Leu | Glu | Val | Glu<br>785   | Leu | Leu | Leu | Ala | Thr<br>790 | Ile | Ser | Glu      | Gln   | Glu<br>795 |     |   |   | ٠. |                          |   |
|        | Leu     | His | Pro | Val | Ser<br>800   | Ala | Arg | Ala | Arg | Val<br>805 |     | Ile | Glu      | Leu   | Pro<br>810 |     |   |   | ,  | بر * * •                 |   |
| * * *. | Leu     | Ser | Ile | Ala | Gly<br>815   | Met | Ala | Ile | Pro | Gln<br>820 |     | Leu | Phe      | Phe   | Ser<br>825 | ē.  | * | : |    |                          |   |
| *      | Gļy     | Val | Val | Arg | Gly<br>830   | Glu | Arg | Ala | Met | Gln<br>835 |     | Glu | Arg      | Asp   | Val<br>840 | ,'  |   |   |    |                          |   |
|        | Gly     | Ser | Lys | Val | Lys<br>845   | Tyr | Glu | Val | Thr | Val<br>850 |     | Asn | Gln      | Gly   | Gln<br>855 | *   |   |   |    |                          |   |
|        | Ser     | Leu | Arg | Thr | Leu<br>860   | Gly | Ser | Ala | Phe | Leu<br>865 |     | Ile | Met      | Trp   | Pro<br>870 |     |   |   |    |                          |   |
|        | His     | Glu | Ile | Ala | Asn<br>875   | Gly | Lys | Trp | Leu | Leu<br>880 |     | Pro | Met      | Gln   | Val<br>885 | • . |   |   |    |                          |   |
|        | Glu     | Leu | Glu | Gly | Gly<br>890   | Gln | Gly | Pro | Gly | Gln<br>895 |     | Gly | Leu      | Cys   | Ser<br>900 |     |   |   |    | •                        |   |
|        | Pro     | Arg | Pro | Asn | Ile<br>905   | Leu | His | Leu | Asp | Val<br>910 |     | Ser | Arg      | Asp   | Arg<br>915 |     |   |   |    |                          | , |
|        | Arg     | Arg | Arg | Glu | Leu<br>920   |     | Pro | Pro | Glu | Gln<br>925 |     | Glu | Pro      | Gly   | Glu<br>930 |     |   |   |    |                          |   |
|        | Arg     | Gln | Glu | Pro | Ser<br>935   |     | Ser | Trp | Trp | Pro<br>940 |     | Ser | Ser      | · Ala | Glu<br>945 |     |   | • |    | *                        |   |
|        | Lys     | Lys | Lys | Asn |              | Thr | Leu | Asp | Cys | Ala<br>955 |     | Gly | Thr      | Ala   | Asn<br>960 |     |   |   |    |                          |   |
| •      |         |     |     |     |              |     |     |     |     |            |     |     |          |       |            |     |   |   |    |                          |   |
|        |         |     |     |     |              |     |     |     |     |            |     |     |          |       |            |     |   |   |    |                          |   |

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Cys Val Val Phe Ser Cys Pro Leu Tyr Ser Phe Asp Arg Ala Ala
               965
                                  970-
Val Leu His Val Trp Gly Arg Leu Trp Asn Ser Thr Phe Leu Glu
               980 -
Glu Tyr Ser Ala Val Lys Ser Leu Glu Val Ile Val Arg Ala Asn
               995
                                 1000
Ile Thr Val Lys Ser Ser Ile Lys Asn Leu Met Leu Arg Asp Ala
                              1015
              1010
Ser Thr Val Ile Pro Val Met Val Tyr Leu Asp Pro Met Ala Val
              1025
                                 1030
Val Ala Glu Gly Val Pro Trp Trp Val Ile Leu Leu Ala Val Leu
     1050
Ala Gly Leu Leu Val Leu Ala Leu Leu Val Leu Leu Trp Lys
              1055
                             1060
Met Gly Phe Phe Lys Arg Ala Lys His Pro Glu Ala Thr Val Pro
                                  1075 ·
Gln Tyr His Ala Val Lys Ile Pro Arg Glu Asp Arg Gln Gln Phe
                                  1090
             1085
Lys Glu Glu Lys Thr Gly Thr Ile Leu Arg Asn Asn Trp Gly Ser
                                  1105
               1100
Pro Arg Arg Glu Gly Pro Asp Ala His Pro Ile Leu Ala Ala Asp
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<211> 436

<212> PRT

<213> Homo sapiens

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Cys Ser Gln Ser Leu Ala Ala Ala Ala Ala Val Ala Ala Ala Gly
20 25 30

Gly Arg Ser Asp Gly Gly Asn Phe Leu Asp Asp Lys Gln Trp Leu

| Thr | Thr | Ile | Ser | Gln<br>50  | Tyr | Asp | Lys | Glu | Val<br>55  | Gly | Gln  | Trp  | Asn | Lys<br>60  |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|------|------|-----|------------|
| Phe | Arg | Asp | Glu | Val<br>65  | Glu | Asp | Asp | Tyr | Phe<br>70  | Arg | Thr  | Trp. | Ser | Pro<br>75  |
| Gly | Lys | Pro | Phe | Asp<br>80  | Gln | Ala | Leu | Asp | Pro<br>85  | Ala | Lys  | Asp  | Pro | Cys<br>90  |
| Leu | Lys | Met | Lys | Cys<br>95  | Ser | Arg | His | Lys | Val<br>100 | Cys | Ile  | Ala  | Gln | Asp<br>105 |
| Ser | Gln | Thr | Ala | Val<br>110 | Cys | Ile | Ser | His | Arg<br>115 | Arg | Leu  | Thr  | His | Arg<br>120 |
| Met | Lys | Glu | Ala | Gly<br>125 |     | Asp | His | Arg | Gln<br>130 | Trp | Arg  | Gly  | Pro | Ile<br>135 |
| Leu | Ser | Thr | Cys | Lys<br>140 | Gln | Cys | Pro | Val | Val<br>145 | Tyr | Pro  | Ser  | Pro | Val<br>150 |
| Cys | Gly | Ser | Asp | Gly<br>155 | His | Thr | Tyr | Ser | Phe<br>160 | Gln | Cys  | ŗys  | Leu | Glu<br>165 |
| Tyr | Gln | Ala | Cys | Val<br>170 | Leu | Gly | Lys | Gln | Ile<br>175 | Ser | Val  | Lys  | Cys | Glu<br>180 |
| Gly | His | Cys | Pro | Cys<br>185 | Pro | Ser | Asp | Lys | Pro<br>190 | Thr | ,Ser | Thr  | Ser | Arg<br>195 |
| Asn | Val | Lys | Arg | Ala<br>200 | Cys | Ser | Asp | Leu | Glu<br>205 | Phe | Arg  | Glu  | Val | Ala<br>210 |
| Asn | Arg | Leu | Arg | Asp<br>215 | Trp | Phe | Lys | Ala | Leu<br>220 | His | Glu  | Ser  | Gly | Ser<br>225 |
| Gln | Asn | Lys | Lys | Thr<br>230 | Lys | Thr | Leu | Leu | Arg<br>235 | Pro | Glu  | Arg  | Ser | Arg<br>240 |
| Phe | Asp | Thr | Ser | Ile<br>245 | Leu | Pro | Ile | Cys | Lys<br>250 | Asp | Ser  | Leu  | Gly | Trp<br>255 |
| Met | Phe | Asn | Arg | Leu<br>260 | Asp | Thr | Asn | Tyr | Asp<br>265 |     | Leu  | Leu  | Asp | Gln<br>270 |
| Ser | Glu | Leu | Arg | Ser<br>275 |     | Tyr | Leu | Asp | Lys<br>280 |     | Glu  | Gln  | Cys | Thr<br>285 |
| Lys | Ala | Phe | Phe | Asn<br>290 |     | Cys | Asp | Thṛ | Tyr<br>295 |     | Asp  | Ser  | Leu | Ile<br>300 |
| Ser | Asn | Asn | Glu | Trp<br>305 |     | Tyr | Суѕ | Phe | Gln<br>310 |     | Gln  | Gln  | Asp | Pro<br>315 |
| Pro | Cys | Gln | Thr | Glu        | Leu | Ser | Asn | Ile | Gln        | Lys | Arg  | Gln  | Gly | Val        |

320

Lys Lys Leu Leu Gly Gln Tyr Ile Pro Leu Cys Asp Glu Asp Gly 335 340 345

Tyr Tyr Lys Pro Thr Gln Cys His Gly Ser Val Gly Gln Cys Trp 350 355 360

Cys Val Asp Arg Tyr Gly Asn Glu Val Met Gly Ser Arg Ile Asn 365 370 375

Gly Val Ala Asp Cys Ala Ile Asp Phe Glu Ile Ser Gly Asp Phe 380 385 390

Ala Ser Gly Asp Phe His Glu Trp Thr Asp Asp Glu Asp Asp Glu 395 400 405

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Glu Cys Phe Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile 50 55 60

Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe Glu Gln Arg Lys 80 Ser Asp Gly Val His Thr Val Glu Thr Glu Val Gly Asp Tyr Met 100 Phe Cys Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Lys Val Ile 115 Phe Phe Glu Leu Ile Leu Asp Asn Met Gly Glu Gln Ala Gln Glu 125 130 Gln Glu Asp Trp Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile Asn Ser Ile Lys Ser 160 Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu Leu Arg Ala Phe 175 Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe Asp Arg Val 190 Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val Val Ser. 205 200 Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys Arg 215 Lys Ser Arg Thr <210> 448 <211> 23 <212> DNA <213> Artificial Sequence <220> <223> Synthetic oligonucleotide probe <400> 448. cccagcaggg ctgggcgaca aga 23 <210> 449 <211> 23 <212> DNA <213> Artificial Sequence <223> Synthetic oligonucleotide probe

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 Ala Tyr Gly Ser Pro Cys Tyr Ala Leu Phe Leu Ser Pro Lys Ser
 Trp Met Asp Ala Asp Leu Ala Cys Gln Lys Arg Pro Ser Gly Lys
 Leu Val Ser Val Leu Ser Gly Ala Glu Gly Ser Phe Val Ser Ser
 Leu Val Arg Ser Ile Ser Asn Ser Tyr Ser Tyr Ile Trp Ile Gly
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 Leu His Asp Pro Thr Gln Gly Ser Glu Pro Asp Gly Asp Gly Trp
                                    115
 Glu Trp Ser Ser Thr Asp Val Met Asn Tyr Phe Ala Trp Glu Lys
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 Asn Pro Ser Thr Ile Leu Asn Pro Gly His Cys Gly Ser Leu Ser
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 Arg Ser Thr Gly Phe Leu Lys Trp Lys Asp Tyr Asn Cys Asp Ala
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Asn Glu Thr Met Cys Lys Thr Thr Leu Tyr Ser Arg Glu Ile Val
50 55 60

Tyr Pro Phe Gln Gly Asp Ser Thr Val Thr Lys Ser Cys Ala Ser 65 70 75

Lys Cys Lys Pro Ser Asp Val Asp Gly Ile Gly Gln Thr Leu Pro 80 85 90

Val Ser Cys Cys Asn Thr Glu Leu Cys Asn Val Asp Gly Ala Pro 95 100 105

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| Met<br>1 | Met   | Ala               | Leu | Gly<br>5    | Ala   | Ala  | Gly   | Ala | Thr<br>10    | Arg | Val        | Phe   | Val      | Ala<br>15   |
| Met      | Val   | Ala               | Ala | Ala<br>20   | Leu   | Gly  | Gly   | His | Pro<br>25    | Leu | Leu        | Gly   | Val<br>· | Ser<br>30   |
| Ala      | Thr   | Leu<br>·          | Asn | Ser<br>. 35 | Val   | Leu  | Asn   | Ser | Asn<br>40    | Ala | Ile        | Lys   | Asn      | Leu<br>45   |
| Pro      | Pro   | Pro               | Leú | Gly<br>50   | Gly   | Ala  | Ala   | Gly | His<br>55    | Pro | Gly        | Ser   | Ala      | Val<br>. 60 |
| _ Ser    | _Ala  | Ala               | Pro | Gly<br>65   | -Ile- | -Leu | -Tyr- | Pro | -G1·y<br>.70 | Gly | ·<br>-Asn- | -Lys- | Tyr      | Gln-75      |
| Thr      | Ile   | Asp               | Asn | Tyr<br>80   | Gln   | Pro  | Tyr   | Pro | Cys<br>85    | Ala | Glu        | Asp   | Glu      | Glu<br>90   |
| Cys      | Gly   | Thr               | Asp | Glu<br>95   | Tyr   | Cys  | Ala   | Ser | Pro<br>100   | Thr | Arg        | Gly   | Gly      | Asp<br>105  |
| Ala      | Gly   | Va <sub>.</sub> l | Gln | Ile<br>110  | Cys   | Leu  | Ala   | Cys | Arg<br>115   | Lys | Arg        | Arg   | Lys      | Arg<br>120  |
| Cys      | Met   | Arg               | His | Ala<br>125  | Met   | Cys  | Cys   | Pro | Gly<br>130   | Asn | Tyr        | Cys   | Lys      | Asn<br>135  |
| Gl       | / Ile | Суѕ               | Val | Ser<br>140  | Ser   | Asp  | Gln   | Asn | His<br>145   | Phe | Arg        | Gly   | Glu      | Ile<br>150  |
| Ģl       | ı Glu | Thr               | Ile | Thr<br>155  | Glu   | Ser  | Phe   | Gly | Asn<br>160   | Asp | His        | Ser   | Thr      | Leu<br>165  |
| Ası      | o Gly | Tyr               | Ser | Arg<br>170  | Arg   | Thr  | Thr   | Leu | Ser<br>175   | Ser | Lys        | Met   | Tyr      | His<br>180  |
| Th       | r Lys | Gly               | Gln | Glu<br>185  |       | Ser  | Val   | Cys | Leu<br>190   | Arg | Ser        | Ser   | Asp      | Cys<br>195  |
| Al       | a Ser | Gly               | Leu | Cys<br>200  |       | Ala  | Arg   |     | Phe<br>205   |     | Ser        | Lys   | Ile      | Cys<br>210  |
| Lу       | s Pro | Val               | Leu | Lys<br>215  |       | Gly  | Gln   | Val | Cys<br>220   |     | Lys        | His   | Arg      | Arg<br>225  |
| Ly       | s Gly | / Ser             | His | Gly         |       | Glu  | Ile   | Phe | Gln<br>235   |     | Cys        | Tyr   | Cys      | Gly<br>240  |
| Gl       | u Gly | , Leu             | Ser | Cys<br>245  |       | Ile  | Gln   | Lys | Asp<br>250   |     | His        | Gln   | Ala      | Ser<br>255  |
| As       | n Sei | Ser               | Arc | Leu<br>260  |       | Thr  | Cys   | Gln | Arg<br>265   |     |            |       |          |             |

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Ala Ser Ser Arg Glu Ile Arg Gln Ala Phe Lys Lys Leu Ala Leu 50 55 60

Lys Leu His Pro Asp Lys Asn Pro Asn Asn Pro Asn Ala His Gly
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<sup>&</sup>lt;211> 747 ·

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|                                       | Asp | Phe  | Leu   | Lys | Ile<br>80  | Asn | Arg  | Ala | Tyr   | Glu<br>85    | Val | Leu | Lys | Asp | Glu<br>90  |      |           |           |     |     |           |   |            |
|---------------------------------------|-----|------|-------|-----|------------|-----|------|-----|-------|--------------|-----|-----|-----|-----|------------|------|-----------|-----------|-----|-----|-----------|---|------------|
| R.                                    | Asp | Leu  | Arg   | Lys | Lys<br>95  | Tyr | Asp  | Lys | Tyr   | Gly<br>100   | Glu | Lys | Gly | Leu | Glu<br>105 |      |           |           |     |     |           |   |            |
| ÷                                     | Asp | Asn  | .Gln  | Gly | Gly        | Gln | Tyr  | Glu | Ser   |              | Asn | Tyr | Tyr | Arg |            | ٠.   |           |           |     |     |           |   |            |
|                                       | Asp | Phe  | Gly   | Ile |            | Asp | Asp  | Asp | Pro   | Glu          | Ile | Ile | Thr | Leu | Glu        |      |           |           |     |     |           |   |            |
| ·                                     | Arg | Arg  | Glu   | Phe | 125<br>Asp | Ala | Ala  | Val | Asn   | 130<br>Ser   | Ġly | Glu | Leu | Trp | 135<br>Phe |      |           |           |     |     |           |   |            |
| -(-                                   |     |      |       |     | 140        |     |      |     |       | 145          | 4.0 | His | ٠.  |     | 150        |      |           |           |     | į · | •         |   | ֥          |
|                                       |     | A311 |       |     | 155        |     | ··   |     |       | 160          |     |     |     |     | 165        |      | <u></u> - |           |     |     |           | . <del></del> .                             |            |
|                                       | Pro | Thr  | Trp   | Arg | Asp<br>170 | Phe | Ala  | Lys | Glu   | Val<br>175   | Asp | Gly | Leu | Leu | Arg<br>180 |      |           |           |     |     |           |   | ٠.         |
| *                                     | Ile | Gly  | Ala   | Val | Asn<br>185 | Cys | Gly  | Asp | Asp   | Arg<br>190   | Met | Leu | Cys | Arg | Met<br>195 |      |           |           | ,   |     |           | \$ ***<br>********************************* |            |
|                                       | Lys | Gly  | Val   | Asn | Ser<br>200 | Tyr | Pro  | Ser | Leu   | Phe<br>205   |     | Phe | Arg | Ser | Gly<br>210 |      | ·         |           | •   |     |           | 9   | ag si<br>e |
| · · · · · · · · · · · · · · · · · · · | Met | Ala  | Pro   | Val | Lys<br>215 | Tyr | ·His | Gly | Asp   | Arg<br>220   | Ser | Lys | Glu | Ser | Leu<br>225 |      |           |           |     | 10  |           | •   | · . · · ·  |
|                                       | Val | Ser  | Phe   | Ala | Met<br>230 |     | His  | Val | Arg   | Ser<br>235   |     | Val | Thr | Glu | Leu<br>240 |      |           |           |     | . • | æ         | ٠.  |            |
|                                       | Trp | Thr  | Gly   | Asn | Phe<br>245 | Val | Asn  | Ser | Ile   | Gln<br>250   |     | Ala | Phe | Ala | Ala<br>255 |      | : ···     |           |     |     | • .       |   | e          |
| · · · · · · · · · · · · · · · · · · · | Gly | Ile  | Gly   | Trp | Leu<br>260 |     | Thr  | Phe | Cys   | Ser<br>265   |     | Gly | Gļy | Asp | Cys<br>270 |      |           |           |     | =   | · · · · · |   |            |
|                                       | Leu | Thr  | Ser   | Gln | Thr<br>275 |     | Leu  | Arg | Leu   | Ser<br>280   |     | Met | Leu |     | Leu<br>285 | . ÷. |           |           |     | •   | **        |   | :          |
|                                       | Asn | Ser  | Leu   | Asp | Ala<br>290 |     | Glu  | Ile | Tyr   | Leu<br>295   |     | Val | Íle | His | Asn<br>300 |      |           |           | • . |     | . •       | •   | ,          |
|                                       | Leu | Pro  | Asp   | Phe | Glu<br>305 |     | Leu  | Ser | Ala   | Asn<br>310   |     | Leu | Glu | Asp | Arg<br>315 |      | -         | 1 14<br>1 |     |     | ···       |   |            |
|                                       | Leu | Ala  | His   | His | Arg<br>320 |     | Leu  | Leu | Phe   | Phe<br>325   |     | Phe | Gly | Lys | 330        |      |           |           |     |     |           | •   |            |
| **                                    | Glu | Asn  | Ser   | Asn | Asp<br>335 |     | Glu  | Leu | Lys   | Lys<br>340   |     | Lys | Thr | Leu | Leu<br>345 |      |           |           |     |     |           | 6.7<br>2                                    | * .        |
|                                       | Lys | Asn  | . Asp | His | Ile<br>350 |     | Val  | Gly | ⁄ Arç | 9 Phe<br>355 |     | Cys | Ser | Ser | Ala<br>360 |      |           |           |     |     |           |   | ,          |
|                                       |     |      |       |     |            | •   |      |     |       |              |     |     |     |     |            |      |           |           |     | ` , |           |   | :          |
|                                       |     |      |       |     |            |     |      | ٠,  |       |              |     |     |     |     |            | •    | •         |           |     |     |           |   |            |
| . •                                   |     |      |       |     |            |     |      |     |       |              |     |     | •   |     |            |      |           |           | ٠.  |     |           |   |            |
|                                       | •   |      |       |     |            |     |      |     |       |              |     |     |     |     |            |      |           |           |     |     |           |   | _          |

|                                       | Pro | Asp   | Ile   |       | Ser<br>365   | Asn | Leu   | Tyr   | Val | Phe 370     |     | Pro      | Ser   | Leu | Ala<br>375    |
|---------------------------------------|-----|-------|-------|-------|--------------|-----|-------|-------|-----|-------------|-----|----------|-------|-----|---------------|
|                                       | Val | Phe   | Lys   |       | Gln<br>380   | Gly | Thr   | Lys   | Glu | Tyr<br>385  | Glu | Ile      | His   | His | Gly<br>390    |
|                                       | Lys | Lys   | Ile   | Leu   | Tyr<br>395   | Asp | Ile   | Leu   | Ala | Phe<br>400  | Ala | Lys      | Glu   | Ser | Val<br>405    |
|                                       | Asn | Ser   | His   | Val   | Thr<br>410   | Thr | Leu   | Gly   | Pro | Gln<br>415  | Asn | Phe      | Pro   | Ala | Asn<br>420    |
| •                                     | Asp | Lys   | Glu   | Pro   | Trp<br>425   | Leu | Val   | Asp   | Phe | Phe<br>430  | Ala | Pro      | Trp   | Cys | Pro<br>435    |
|                                       | Pro | Cys   | Arg   |       | Leu<br>440   |     | Pro   | Glu   | Leu | Arg<br>-445 | Arg | Ala      | Ser   | Asn | Leu<br>-450 - |
|                                       | Leu | Tyr   | Gly   | Gln   | Leu<br>455   | Lys | Phe   | Gly   | Thr | Leu<br>460  | Asp | Cys      | Thr   | Val | His<br>465    |
| · · · · · · · · · · · · · · · · · · · | Glu | Gly   | Leu   | Cys   | Asn<br>470   | Met | Tyr   | Asn   | Ile | Gln<br>475  | Ala | Tyr      | Pro   | Thr | Thr<br>480    |
|                                       | Val | Val   | Phe   | Asn   | Gln<br>485   | Ser | Asn   | Ile   | His | Glu<br>490  | Tyr | Glu      | Gly   | His | His<br>495    |
|                                       | Ser | Ala   | Glu   | Gln   | Ile<br>500   | Leu | Glu   | Phe   | Ile | Glu<br>505  | Asp | Leu<br>: | Met   | Asn | Pro<br>510    |
| ·<br>·.                               | Ser | Val   | Val   | Ser   | Leu<br>515   | Thr | Pro   | Thr   | Thr | Phe<br>520  | Asn | Glu      | Leu   | Val | Thr<br>525    |
| :.                                    | Gln | Arg   | Lys   | His   | Asn<br>530   |     | Val   | Trp   | Met | Val<br>535  | Asp | Phe      | Tyr   | Ser | Pro<br>540    |
|                                       | Trp | Cys   | His   | Pro   | Cys<br>545   |     | Val   | Leu   | Met | Pro<br>550  | Glu | Trp      | Lys   | Arg | Met<br>555    |
|                                       | Ala | Arg   | Thr   | Leu   | Thr<br>560   |     | Leu   | ·Ile  | Asn | Val<br>565  | Gly | Ser      | Ile   | Asp | Cys<br>570    |
|                                       | Gln | Gln   | Tyr   | His   | 575          |     | e Cys | : Ala | Gln | Glu<br>580  |     | Val      | Gln   | Arg | Tyr<br>585    |
|                                       | Pro | oʻGlu | ı Ile | e Arg | 9 Phe<br>590 |     | Pro   | ) Pro | Lys | Ser<br>595  |     | Lys      | Ala   | Tyr | Gln<br>600    |
|                                       | Tyr | His   | Ser   | Туг   | 605          |     | Trp   | Asr   | Arg | Asp<br>610  |     | Туг      | Ser   | Leu | Arg<br>615    |
|                                       | Ile | e Trp | Gly   | / Let | 620          |     | e Lei | ı Pro | Glr | val<br>625  |     | Thr      | Asp   | Leu | Thr<br>630    |
| . *                                   | Pro | Glr   | n Thr | Phe   | e Ser<br>635 |     | ı Lys | s Val | Leu | Glr<br>640  |     | / Lys    | , Asn | His | Trp<br>645    |

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                                  655 .
Ala Pro Glu Phe Glu Leu Leu Ala Arg Met Ile Lys Gly Lys Val
               665
                                   670 .
Lys Ala Gly Lys Val Asp Cys Gln Ala Tyr Ala Gln Thr Cys Gln
                                   685
Lys Ala Gly Ile Arg Ala Tyr Pro Thr Val Lys Phe Tyr Phe Tyr
                695
                                   700
Glu Arg Ala Lys Arg Asn Phe Gln Glu Glu Gln Ile Asn Thr Arg
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Asp Ala Lys Ala Ile Ala Ala Leu Ile Ser Glu Lys Leu Glu Thr
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<212> PRT

<213> Homo sapiens

<400> 464

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Tyr Ser Tyr Leu Glu Ser Leu Val Lys Phe Phe Ile Pro Gln Arg 20 25 30

Arg Lys Ser Val Ala Gly Glu Ile Val Leu Ile Thr Gly Ala Gly
35 40 45

His Gly Ile Gly Arg Gln Thr Thr Tyr Glu Phe Ala Lys Arg Gln
50 55 60

Ser Ile Leu Val Leu Trp Asp Ile Asn Lys Arg Gly Val Glu Glu 65 70 75

Thr Ala Ala Glu Cys Arg Lys Leu Gly Val Thr Ala His Ala Tyr 80 85 90

Val Val Asp Cys Ser Asn Arg Glu Glu Ile Tyr Arg Ser Leu Asn 95 100 105

Gln Val Lys Lys Glu Val Gly Asp Val Thr Ile Val Val Asn Asn 110 115 120

Ala Gly Thr Val Tyr Pro Ala Asp Leu Leu Ser Thr Lys Asp Glu 125 130 135

Glu Ile Thr Lys Thr Phe Glu Val Asn Ile Leu Gly His Phe Trp 140 145 150

Ile Thr Lys Ala Leu Leu Pro Ser Met Met Glu Arg Asn His Gly

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155 160 165

His Ile Val Thr Val Ala Ser Val Cys Gly His Glu Gly Ile Pro . 170 Tyr Leu Ile Pro Tyr Cys Ser Ser Lys Phe Ala Ala Val Gly Phe 185 His Arg Gly Leu Thr Ser Glu Leu Gln Ala Leu Gly Lys Thr Gly 200 Ile Lys Thr Ser Cys Leu Cys Pro Val Phe Val Asn Thr Gly Phe 220 Thr Lys Asn Pro Ser Thr Arg Leu Trp Pro Val Leu Glu Thr Asp 230 Glu Val Val Arg Ser Leu Ile Asp Gly Ile Leu Thr Asn Lys Lys 250 Met Ile Phe Val Pro Ser Tyr Ile Asn Ile Phe Leu Arg Leu Gln Lys Phe Leu Pro Glu Arg Ala Ser Ala Ile Leu Asn Arg Met Gln 280 275

Asn Ile Gln Phe Glu Ala Val Val Gly His Lys Ile Lys Met Lys

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gctgtggctg gtgctggggt cggtgttcat gatcctgctg atcatcgtgt 200
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gtgctggcgt gaagcagac gaccttccca gaaaggagac ggagcagccg 400
cctgcgccgg ggagcatgga ggagagcgtg agaggctacg actggtccc 450
gcgcgacgcc cggcgagcc cagaccagg ccggcagcag gcggagcgga 500
ggagcgtgct gcggggcttc tgcgccaact ccagcctggc cttcccacc 550

, =

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Met Thr Lys Ala Arg Leu Phe Arg Leu Trp Leu Val Leu Gly Ser

Val Phe Met Ile Leu Leu Ile Ile Val Tyr Trp Asp Ser Ala Gly

Ala Ala His Phe Tyr Leu His Thr Ser Phe Ser Arg Pro His Thr

Gly Pro Pro Leu Pro Thr Pro Gly Pro Asp Arg Asp Arg Glu Leu

|     |   |        |       | •     |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   | •  |   |    |   |
|-----|---|--------|-------|-------|-----------|------------|-------|------------|---------|----------|------------|------------|---------|--------|-------|--------------|----|---|---|----|---|----|---|
|     |   |        |       |       |           |            |       |            | •       |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     | • |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    | • |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         | -        |            |            |         |        |       |              |    |   |   |    | • |    |   |
|     |   |        |       | _     |           |            |       | 7          | C1      | Dho      | Lovi       | 7.00       | Tuc     | Dho    | T.e.u | Ser          |    |   |   |    |   |    |   |
|     |   | Thr    | Ala   | Asp   | Ser       | Asp<br>65  | val   | Asp        | GIU     | rne      | 70         | АЅР        | гуз     | FIIC   | Deu   | 75           |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         | ,        |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   | Ala    | Gly   | Val   | Lys       |            | Ser   | Asp        | Leu     | Pro      | Arg<br>85  | Lys        | Glu     | Thr    | Glu   | 90<br>90     |    |   |   |    |   |    |   |
|     |   |        |       |       |           | 80         |       |            |         |          |            |            |         |        |       | , 5,0        | ,  |   |   |    |   |    |   |
|     |   | Pro    | Pro   | Ala   | Pro       | Gly        | Ser   | Met        | Glu     | Glu      | Ser        | Val        | Arg     | Gly    | Tyr   | Asp          |    |   |   |    |   |    |   |
|     |   |        |       |       |           | 95         |       |            |         | •        | 100        |            |         |        |       | 105          |    |   |   |    | , |    |   |
|     |   | Trp    | Ser   | Pro   | Arg       | qaA        | Ala   | Arg        | Arg     | Ser      | Pro        | Asp        | Gln     | Gly    | Arg   | Gln          | ٠. |   |   |    |   |    |   |
|     |   |        |       |       | ,         | 110        |       | -          |         |          | 115        |            |         |        |       | 120          |    |   |   |    |   |    |   |
|     |   | C1     | 71.   | C1    | Arg       | 7~~        | Sor   | V = 1      | <br>Len | Ara      | Glv        | Phe        | Cvs     | Ala    | Asn   | Ser          |    |   |   | •  | • |    |   |
|     |   | GIN    | Ala   | GIU   | Arg       | 125        | Ser.  | vai        | пец     | nrg      | 130        | 2,110      |         |        |       | 135          |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            | ,<br>      |         |        |       | Divo         |    |   |   |    |   | ·  |   |
|     |   | Ser    | Leu   | Alā   | 'Phē'     | Pro<br>140 | Thr'  | Lys        | Glü     | Arg      | 145        | Phe        | Asp     | Asp    | ire   | 150          |    |   |   |    |   |    |   |
|     | • |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   | Asn    | Ser   | Glu   | Leu       |            | His   | Leu        | Ile     | Val      | Asp        | Asp        | Arg     | His    | Gly   | Ala<br>165   |    |   |   |    |   |    |   |
| -9- |   |        |       |       |           | 155        |       |            | ٠.      |          | 160        |            |         |        |       | 103          |    |   |   |    |   |    |   |
|     |   | Ile    | Tyr   | Cys   | Tyr       | Val        | Pro   | Lys        | Val     | Ala      | Cys        | Thr        | Asn     | Trp    | Lys   | Arg          |    |   |   |    |   |    |   |
|     |   | -      | -     | -     | · .=      | 170        |       |            |         |          | 175        |            |         |        |       | 180          | •  |   |   |    |   |    |   |
|     |   |        | Mot   | T10   | <br>Val   | T.011      | Ser   | Glv        | Ser     | Leu      | Leu        | His        | Ara     | Glv    | Ala   | Pro          |    |   |   |    |   |    |   |
| ·   |   | Val    | Met   | 116   | Val       | 185        | Ser   | ·OLY       | 501     | Lou      | 190        | •          | 141     | 1      |       | 195          |    |   | * |    |   |    |   |
| •   |   |        |       |       | ٠.        |            | _     |            |         | ٠        | G1         |            | 17.01   | II i e | . 705 |              |    |   | 1 |    |   |    |   |
|     |   | Tyr    | Arg   | Asp   | Pro       | Leu<br>200 | Arg   | Ile        | Pro     | Arg<br>  | 205        | HIS        | vaı     | HIS    | ASI   | Ala<br>210   |    | , |   |    |   |    |   |
|     |   |        | •     |       |           |            |       |            |         |          |            |            |         |        |       |              |    | : |   |    | : | ٠. |   |
|     |   | Ser    | Ala   | His   | Leu       |            | Phe   |            | Lys     | Phe      | Trp        | Arg        | Arg     | Туг    | : Gly | Lys<br>225   |    |   | • |    |   | ÷  |   |
| •   |   |        |       |       |           | 215        |       | ١.         |         |          | 220        | ,          |         |        |       | 223          |    |   |   | *  |   |    |   |
|     | , | Let    | Ser   | Arg   | His       | Leu        | Met   | Lys        | Val     | Lys      | Leu        | Lys        | Lys     | туз    | Thr   | Lys          |    | , |   | н. |   |    | • |
|     |   |        |       |       |           | 230        |       |            |         |          | 235        |            |         |        |       | 240          |    |   |   |    |   |    |   |
|     |   | Phe    | í.e.  | Phe   | Val       | Ara        | Asp   | Pro        | Phe     | :<br>Val | . Arc      | Leu        | Ile     | Sei    | . Ala | Phe          |    |   |   | ٠. | • |    |   |
|     |   | , 1110 | . 100 |       | , , , , , | 245        |       |            |         |          | 250        | )          | :       |        |       | 255          |    |   |   |    |   |    |   |
|     |   |        | _     | _     |           | <br>       | T     | ·<br>- Cl. | , nat   |          | . 61.      | , Phe      | Тут     | - Arc  | T.V.S | s Phe        |    |   |   |    |   |    |   |
| •   |   | Arg    | g.Ser | . гуз | Pne       | 260        | Leu   | GIL        | HSI.    | ı Gıt    | 265        | 5          | . 1 9 1 |        | 9 -1. | 270          |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            |            |         |        | •     |              |    |   |   |    |   |    |   |
|     |   | Ala    | a Val | l Pro | ) Met     | Leu        | Arg   | Leu        | туг     | : Ala    | AST<br>280 | n His<br>N | i l'nı  | : Se   | r Le  | 285          | A  | • |   |    |   |    |   |
|     |   |        | •     | *.    |           | 275        |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   | Ala    | a Sei | c Ala | a Arg     | Glu        | Ala   | Phe        | e Arc   | g Ala    | a Gly      | y Lev      | ı Ly:   | s Va   | l Se  | r Phe        | ·  |   |   |    |   |    |   |
|     |   |        |       |       |           | 290        |       |            |         |          | 295        | •          |         |        |       | 300          |    |   |   |    |   |    |   |
|     |   | Ala    | a Ası | n Phe | e Ile     | Gln        | Туг   | : Le       | ı Lei   | ı Ası    | o Pro      | o His      | Th:     | r Gl   | u Ly  | s Leu        |    |   |   | ·  |   |    |   |
| •   |   |        |       |       |           | 305        | , .   |            |         |          | 310        | 0          |         |        |       | 315          |    |   |   |    |   |    |   |
|     |   | 70.7   | Dei:  | o Dh  | - 7ar     | . Gl.:     | . Hie | : ጥrr      | n Ard   | r Gli    | n Vai      | 1 Tv:      | r Ar    | a Le   | u Cy  | s His        |    |   |   |    |   |    |   |
|     |   | AL     | a.Pr  | o Pne | e ASI     | 320        |       |            | 7 711.  | 9 01.    | 32         | 5          |         | J      | -     | 330          |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       | _          | -       | ••-      |            | ·          | - T -   |        |       | <b>~</b> Tou |    |   |   |    |   |    |   |
|     |   | Pr     | o Cy  | s Gl: | n Ile     |            |       | c Ası      | o Phe   | e va.    | 34         | у<br>У гу  | з ге    | u GI   | u III | r Leu<br>345 |    |   |   |    |   |    |   |
|     |   |        |       |       |           | 335        |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       | ,          |         |          |            |            |         | ٠.     |       |              |    |   |   |    |   |    |   |
|     |   |        |       |       |           |            |       |            |         |          |            |            |         |        |       |              |    |   |   |    |   |    |   |

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Gln Leu Arg Phe Pro Pro Ser Tyr Arg Asn Arg Thr Ala Ser Ser 365 370 375

Trp Glu Glu Asp Trp Phe Ala Lys Ile Pro Leu Ala Trp Arg Gln 380 385 . 390

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200

205

Leu Ala Gln Pro Leu Gly Arg Met Gly Gln Pro Ala Glu Val Gly 225

Ala Ala Ala Val Phe Leu Ala Ser Glu Ala Asn Phe Cys Thr Gly 230 235 240

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Gly Gln Gly Arg Pro Gly Pro Leu Ala Pro Gly Pro His Gln Val 35 40

Pro Leu Asp Leu Val Ser Arg Met Lys Pro Tyr Ala Arg Met Glu
50 55 60

Glu Tyr Glu Arg Asn Ile Glu Glu Met Val Ala Gln Leu Arg Asn
65 70 75

Ser Ser Glu Leu Ala Gln Arg Lys Cys Glu Val Asn Leu Gln Leu 80 85 90

Trp Met Ser Asn Lys Arg Ser Leu Ser Pro Trp Gly Tyr Ser Ile 95 100 105

Asn\_His\_Asp\_Pro\_Ser\_Arg\_Ile\_Pro\_Val\_Asp\_Leu\_Pro\_Glu\_Ala\_Arg\_ 110 115 120

Cys Leu Cys Leu Gly Cys Val Asn Pro Phe Thr Met Gln Glu Asp 125 130 135

Arg Ser Met Val Ser Val Pro Val Phe Ser Gln Val Pro Val Arg 140 145 150

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Arg Tyr Arg Gly Pro Gly Ile Phe Glu Asp Leu Gln Asn Tyr Ile 125 130 135

Leu Glu Lys Lys Trp Gln Ser Val Glu Pro Leu Thr Gly Trp Lys 140 145 150

Ser Pro Ala Ser Leu Thr Met Ser Gly Met Ala Gly Leu Phe Ser 155 160 165

Ile Ser Gly Lys Ile Trp His Leu His Asn Tyr Phe Thr Val Thr 170 Leu Gly Ile Pro Ala Trp Cys Ser Tyr Val Phe Phe Val Ile Ala 190 Thr Leu Val Phe Gly Leu Phe Met Gly Leu Val Leu Val Val Ile 200 Ser Glu Cys Phe Tyr Val Pro Leu Pro Arg His Leu Ser Glu Arg 215 Ser Glu Gln Asn Arg Arg Ser Glu Glu Ala His Arg Ala Glu Gln 235 Leu Gln Asp Ala Glu Glu Glu Lys\_Asp Asp Ser Asn Glu Glu Glu -250 Asn Lys Asp Ser Leu Val Asp Asp Glu Glu Glu Lys Glu Asp Leu Gly Asp Glu Asp Glu Ala Glu Glu Glu Glu Glu Glu Asp Asn Leu 275 Ala Ala Gly Val Asp Glu Glu Arg Ser Glu Ala Asn Asp Gln Gly <sup>,</sup> 290 Pro Pro Gly Glu Asp Gly Val Thr Arg Glu Glu Val Glu Pro Glu 305 Glu Ala Glu Glu Gly Ile Ser Glu Gln Pro Cys Pro Ala Asp Thr 320 Glu Val Val Glu Asp Ser Leu Arg Gln Arg Lys Ser Gln His Ala 340 335 Asp Lys Gly Leu <210> 473 <211> 24 <212> DNA <213> Artificial Sequence

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Leu His Tyr Lys Pro Thr Pro Asp Leu Arg Ile Ser Ile Glu Asn 60

Ser Glu Glu Ala Leu 65

Thr Val His Ala Pro Phe Pro Ala Ala His 70

Pro Ala Ser Arg Ser Phe Pro Asp Pro Arg Gly Leu Tyr His Phe

|    |   |    | Cys | Leu | Tyr | Trp | Asn<br>95  | Arg  | His | A·la | Gly | Arg<br>100  | Leu | His | Leu  | Leu         | Tyr<br>105  |   |
|----|---|----|-----|-----|-----|-----|------------|------|-----|------|-----|-------------|-----|-----|------|-------------|-------------|---|
|    |   |    | Gly | Lys | Arg | Asp | Phe        | Leu' | Leu | Ser  | Asp | Lys<br>115  | Ala | Ser | Ser  | Leu         | Leu<br>120  |   |
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|    |   |    | Leu | Ala | Thr | Ser | Val<br>140 | Thr  | Ser | Trp  | Trp | Ser.<br>145 | Pro | Gln | Asn  | Ile         | Ser<br>150  |   |
|    |   |    | Leu | Pro | Ser | Ala | Ala<br>155 | Ser  | Phe | Thr  | Phe | Ser<br>160  | Phe | His | Ser  | Pro         | Pro<br>165  |   |
|    |   | _  | His | Thr | Ala | Ala | His<br>170 |      | Ala | Ser  | Val | Asp<br>175  | Met | Cys | Glu  | Le <u>u</u> | Lys<br>180  |   |
|    |   |    | Arg | Asp | Leu |     | Leu<br>185 | Leu  | Ser | Gln  | Phe | Leu<br>190  | Lys | His | Pro  | Gln         | Lys<br>195  |   |
|    |   | 12 | Ala | Ser | Arg | Arg | Pro<br>200 | Ser  | Ala | Ala  | Pro | Ala<br>205  | Ser | Gln | Gln  | Leu         | Gln<br>210  |   |
|    |   |    | Ser | Leu | Glu | Ser | Lys<br>215 |      | Thr | Ser  | Val | Arg<br>220  | Phe | Met | Gly  | Asp         | Met<br>225  |   |
|    | • |    |     |     |     |     | 230        |      |     |      |     | Ala<br>235  |     |     |      |             | 240         |   |
|    |   |    |     |     |     |     | 245        |      |     |      |     | His<br>250  |     |     |      |             | 255         |   |
| .* |   |    |     |     |     |     | 260        |      |     |      |     | 265         |     |     |      |             | Pro<br>270  |   |
|    |   |    |     |     |     |     | 275        |      |     |      |     | Arg<br>280  | •   |     |      |             | 285         |   |
|    |   |    |     |     |     |     | 290        |      |     | ٠.   |     | Ser<br>295  |     |     |      |             | 300         | * |
|    |   |    |     |     |     |     | 305        |      |     |      |     | Glu<br>310  |     |     |      |             | 315         |   |
|    | • | ٠  |     |     |     |     | 320        |      |     |      |     | Leu<br>325  | •   |     |      |             | 330         |   |
|    | • |    |     |     |     |     | .335       |      |     |      |     | 340         |     |     |      |             | Gln<br>345. | • |
|    |   |    |     |     |     |     | 350        | ٠. ' | •   |      |     | 355         |     | •   |      |             | 360         | 1 |
|    |   |    | Trp | ser | ser | ATS | 365        |      | GIU | ini  | val | 370         |     | GIU | 1111 | O111        | Thr<br>375  |   |

| Ser   | Cys   | Phe   | Cys   | Asn<br>380   | His  | Leu   | Thr   | Tyr   | Phe<br>385   | Ala   | Val | Leu  | Met   | Val<br>390 <sup>′</sup> |   |
|-------|-------|-------|-------|--------------|------|-------|-------|-------|--------------|-------|-----|------|-------|-------------------------|---|
| Ser   | Ser   | Val   | Glu   | Val<br>395   | Asp  | Ala   | Val   | His   | Lys<br>400   | His   | Tyr | Leu  | Ser   | Leu<br>405              |   |
| Leu   | Ser   | Tyr   | Val   | Gly<br>410   |      | Val   | Val   | Ser   | Ala<br>415   | Leu   | Ala | Cys  | Leu   | Val<br>420              |   |
| Thr   | Ile   | Ala   | Ala   | Tyr<br>425   | Leu  | Cys   | Ser   | Arg   | Val<br>430   | Pro   | Leu | Pro  | Cys   | Arg<br>435              |   |
| Arg   | Lys   | Pro   | Arg   | Asp<br>440   | Tyr  | Thr   | Ile   | Lys   | Val<br>445   | His   | Met | Asn  | Leu   | Leu<br>450              |   |
| -Leu- | Ala   | -Val  | ·Phe· | -Leu<br>455  | -Leu | Asp   | -Thr  | Ser   | Phe<br>460   | -Leu- | Leu | -Ser | Gŀu   | Pro -<br>465            | - |
| Val   | Ala   | Leu   | Thr   | Gly<br>470   | Ser  | Glu   | Aļa   | Gly   | Cys<br>475   | Arg   | Ala | Ser  | Ala   | Ile<br>480              |   |
| Phe   | Leu   | His   | Phe   | Ser<br>485   | Leu  | Leu   | Thr   | Cys   | Leu<br>490   | Ser   | Trp | Met  | Gly   | Leu<br>495              |   |
| Glu   | Gly   | Tyr   | Asn   | Leu<br>500   | Tyr  | Arg   | Leu   | Val   | Val<br>505   | Glu   | Val | Phe  | Gly   | Thr<br>510              |   |
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| Phe   | Pro   | Ile   | Phe   | Leu<br>530   |      | Thr   | Leu   | Val   | Ala<br>535   | Leu   | Val | Asp  | Val   | Asp<br>540              |   |
| Asn   | Tyr   | Gly   | Pro   | Ile<br>545   |      | Leu   | Ala   | Val   | His<br>550   | Arg   | Thr | Pro  | Glu   | Gly<br>555              |   |
| Val   | Ile   | Туг   | Pro   | Ser<br>560   |      | Cys   | Trp   | Ile   | Arg<br>565   |       | Ser | Leu  | Val   | Ser<br>570              |   |
| Tyr   | Ile   | Thr   | Asn   | Leu<br>575   |      | Leu   | Phe   | Ser   | Leu<br>580   |       | Phe | Leu  | Phe   | Asn<br>585              |   |
| Met   | : Ala | Met   | : Leu | Ala<br>590   |      | Met   | . Val | Val   | Gln<br>595   |       | Leu | Arg  | Leu   | Arg                     |   |
| Pro   | His   | Thi   | Glr   | Lys<br>605   |      | Ser   | His   | Val   | Leu<br>610   |       | Leu | Leu  | Gly   | Leú<br>615              |   |
| Sei   | . Lev | ı Val | l Let | 1 Gly<br>620 |      | Pro   | Trp   | Ala   | Leu<br>625   |       | Phe | Phe  | Ser   | Phe<br>630              |   |
| Ala   | a Ser | c Gly | y Thi | 635          |      | ı Lev | ı Val | . Val | . Leu<br>640 |       | Leu | Phe  | e Ser | 1le<br>645              |   |
| Ile   | e Thi | r Se: | r Phe | e Glr<br>650 |      | y Phe | e Leu | ılle  | Phe 655      | e Ile | Trp | Туг  | Trp   | Ser.<br>660             |   |

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Pro Arg Phe Pro His Thr Tyr Pro Arg Asn Thr Val Leu Val Trp
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Leu Val Glu Ile Asp Phe Arg Cys Asn Cys Val Pro Ile Pro Leu Gly Ser Lys Asn Asn Met Cys Ile Lys Arg Leu Gln Ile Lys Pro

110 Arg Ser Phe Ser Gly Leu Thr Tyr Leu Lys Ser Leu Tyr Leu Asp

125 130

Gly Asn Gln Leu Leu Glu Ile Pro Gln Gly Leu Pro Pro Ser Leu 140

Gln Leu Leu Ser Leu Glu Ala Asn Asn Ile Phe Ser Ile Arg Lys 155

Glu Asn Leu Thr Glu Leu Ala Asn Ile Glu Ile Leu Tyr Leu Gly .175 170

Gln Asn Cys Tyr Tyr Arg Asn Pro Cys Tyr Val Ser Tyr Ser Ile 185

11

|     | Glu Lys Asp Ala | Phe Léu Asn Leu Thr<br>200          | Lys Leu Lys Val Leu Ser<br>205 210                       |                                       |
|-----|-----------------|-------------------------------------|--|---------------------------------------|
|     | Leu Lys Asp Asn | Asn Val Thr Ala Val                 | Pro Thr Val Leu Pro Ser<br>220 225                       |                                       |
|     | Thr Leu Thr Glu | Leu Tyr Leu Tyr Asn<br>230          | Asn Met Ile Ala Lys Ile<br>235 240                       |                                       |
|     | Gln Glu Asp Asp | Phe Asn Asn Leu Asn<br>245          | Gln Leu Gln Ile Leu Asp<br>250 255                       |                                       |
|     | Leu Ser Gly Asn | Cys Pro Arg Cys Tyr<br>260          | Asn Ala Pro Phe Pro Cys<br>265 270                       | · · · · · · · · · · · · · · · · · · · |
|     |                 | 275                                 | Gln-Ile Pro-Val Asn Ala 280 285                          |                                       |
|     |                 | 290                                 | Leu Arg Leu His Ser Asn<br>295 300                       |                                       |
|     |                 | 305                                 | Phe Lys Asn Ile Asn Lys 310 315                          |                                       |
|     |                 | 320                                 | Phe Leu Ala Lys Glu Ile<br>325 330                       |                                       |
| . ' |                 | 335                                 | Pro Ser Leu Ile Gln Leu 340 345                          |                                       |
|     | :               | 350                                 | Val Tyr Arg Ala Ser Met 355 360  Lys Ser Leu Lys Ile Leu |                                       |
|     |                 | 365                                 | 370 375  Leu Lys Ser Phe Asn Leu                         |                                       |
|     |                 | 380                                 | 385 390 Glu Val Leu Asp Leu Gly                          |                                       |
|     | Thr Asn Phe Ile | 395<br>e Lys Ile Ala Asn Leu        | 400 405  Ser Met Phe Lys Gln Phe                         |                                       |
|     | Lys Arg Leu Lys |                                     | 415 420<br>Val Asn Lys Ile Ser Pro                       | *                                     |
|     | Ser Gly Asp Ser |                                     | 430 435<br>Cys Ser Asn Ala Arg Thr                       |                                       |
|     | Ser Val Glu Ser |                                     | Leu Glu Gln Leu His Tyr                                  | * . *                                 |
|     | Phe Arg Tyr Asp | 455<br>p Lys Tyr Ala Arg Ser<br>470 | 460 465<br>Cys Arg Phe Lys Asn Lys<br>475 480            |                                       |
|     |                 |                                     |  |                                       |

| Glu       | Ala | Ser   | Phe  | Met<br>485 | Ser | Val | Asn   | Glu   | Ser<br>490  | Cys  | Tyr | Lys   | Tyr  | Gly<br>495 |                                       |
|-----------|-----|-------|------|------------|-----|-----|-------|-------|-------------|------|-----|-------|------|------------|---------------------------------------|
| Gln       | Thr | Leu   | Asp  | Leu<br>500 | Ser | Lys | Asn   | Ser   | Ile<br>505  | Phe  | Phe | Val   | Lys  | Ser<br>510 |                                       |
| Ser       | Asp | Phe   | Gln  | His<br>515 | Leu | Ser | Phe   | Leu   | Lys<br>520  | Cys  | Leu | Asn   | Leu  | Ser<br>525 | ·<br>·                                |
| Gly       | Asn | Leu   | Ile  | Ser<br>530 | Gln | Thr | Leu   | Asn   | Gly<br>535  | Ser  | Glu | Phe   | Gln  | Pro<br>540 | • .                                   |
| Leu       | Ala | Glu   | Leu  | Arg<br>545 | Tyr | Leu | Asp   | Phe   | Ser<br>550  | Asn  | Asn | Arg   |      | Asp<br>555 | · · · · · · · · · · · · · · · · · · · |
| <br>- Leu | Leu | His   | Ser- | Thr<br>560 | Ala | Phe | Glu   | Glu-  | -Leu<br>565 | -His | Lys | -Leu  | Glu  | Val<br>570 |                                       |
| Leu       | Asp | İle   | Ser  | Ser<br>575 | Asn | Ser | His   | Tyr   | Phe<br>580  | Gln  | Ser | Glu   | Gly  | Ile<br>585 |                                       |
| Thr       | His | Met   | Leu  | Asn<br>590 | Phe | Thr | Lys   | Asn   | Leu<br>595  |      | Val | Leu   | Gln  | Lys<br>600 |                                       |
| Leu       | Met | Met   | Asn  | Asp<br>605 | Asn | Asp | Ile   | Ser   | Ser<br>610  |      | Thr | Ser   | Arg  | Thr<br>615 |                                       |
| Met       | Glu | Ser   | Glu  | Ser<br>620 | Leu | Arg | Thr   | Leu   | Glu<br>625  |      | Arg | Gly   | Asn  | His<br>630 |                                       |
|           | _   |       |      | 635        | •   |     |       |       | 640         |      |     |       |      | Leu<br>645 |                                       |
|           |     |       |      | 650        |     |     |       |       | 655         |      |     |       |      | Asn<br>660 |                                       |
|           |     |       |      | 665        |     |     |       |       | 670         |      |     |       |      | Pro<br>675 |                                       |
|           |     |       |      | 680        |     |     |       |       | 685         |      |     |       |      | Phe<br>690 |                                       |
|           |     | _     | _    | 695        |     |     |       | ,     | 700         |      |     |       |      | 705        |                                       |
|           |     |       |      | 710        |     |     |       |       | 715         | ,    |     |       |      | 720        | · · · · · · · · · · · · · · · · · · · |
| •         |     | _     |      | 725        |     |     |       |       | 730         | )    |     |       |      | 735        |                                       |
|           |     |       |      | 740        |     |     |       |       | 745         | •    |     |       | ·    | 750        |                                       |
| Tyr       | reu | . Asp | rien | 755        |     | AST | г тАг | , TTE | 760         |      | 116 | : GIN | , ту | 765        |                                       |
|           |     |       |      |            |     |     |       |       |             |      |     |       |      |            | ·                                     |
|           |     |       |      |            |     |     |       |       |             |      |     |       |      |            |                                       |

|     |     |       |        |               |      |     |       |       |                         |      |       |      |       | •                       |
|-----|-----|-------|--------|---------------|------|-----|-------|-------|-------------------------|------|-------|------|-------|-------------------------|
| Ser | Phe | Pro   | Glu    | Asn<br>770    | Val  | Leu | Asn   | Asn   | Leu <sup>.</sup><br>775 | Lys  | Met   | Leu  | Leu   | Leu<br>780              |
| His | His | Asn   | Arg    | Phe 785       | Leu  | Cys | Thr   | Cys   | Asp<br>790              | Ala  | Val   | Trp  | Phe   | Val <sup>-</sup><br>795 |
| Trp | Trp | Val   | Asn    | His<br>800    | Thr  | Glu | Val   | Thr   | Ile<br>805              | Pro  | Tyr   | Leu  | Ala   | Thr<br>810              |
| Asp | Val | Thr   | Cys    | Val<br>815    | Gly  | Pro | Gly   | Ala   | His<br>820              | Lys  | Gly   | Gln  | Ser   | Val<br>825              |
| Ile | Ser | Leu   | Asp    | Leu<br>830    | Tyr  | Thr | Суз   | Glu   | Leu<br>835              | Asp  | Leu   | Thr  | Asn   | Leu<br>840              |
| Ile | Leu | Phe   | Ser    | Leu<br>845    | Ser- | Ile | -Ser  | Val   | Ser<br>850              | -Leu | Phe   | -Leu | -Met- | Val .<br>855            |
| Met | Met | Thr   | Ala    | Ser<br>860    | His  | Leu | Tyr   | Phe   | Trp<br>865              | Asp  | Val   | Trp  | Tyr   | Ile<br>870              |
| Tyr | His | Phe   | Cys    | Lys<br>875    | Ala  | Lys | Ile   | Lys   | Gly<br>880              |      | Gln   | Arg  | Leu   | Ile<br>885              |
| Ser | Pro | Asp   | Cys    | Cys<br>890    | Tyr  | Asp | Ala   | Phe   | Ile<br>895              |      | Tyr   | Asp  | Thr   | Lys<br>900              |
| Asp | Pro | Ala   | Val    | Thr<br>905    | Glu  | Trp | Val   | Leu   | Ala<br>910              |      | Leu   | Val  | Ala   | Lys<br>915              |
| Leu | Glu | Asp   | Pro    | Arg<br>920    | Glu  | Lys | His   | Phe   | Asn<br>925              | Leu  | Cys   | Leu  | Glu   | Glu<br>930              |
| Arg | Asp | Trp   | Leu    | Pro<br>935    | Gly  | Gln | Pro   | Val   | Leu<br>940              |      | Asn   | Leu  | Ser   | Gln<br>945              |
| Ser | Ile | Gln   | Leu    | Ser<br>950    | Lys  | Lys | Thr   | Val   | Phe<br>955              |      | Met   | Thr  | Asp   | Lys<br>960              |
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| Gln | Arg | J Leu | Met    | Asp<br>980    |      | Lýs | val   | Asp   | 985                     |      | : Ile | Leu  | Ile   | Phe<br>990              |
| Leu | Glu | ı Lys | Pro    | 995           |      | Lys | Ser   | Lys   | Phe<br>1000             |      | Gln   | Leu  | Arg   | Lys<br>1005             |
| Arg | Lev | ı Cys | Gly    | / Ser<br>1010 |      | Val | Lev   | Glu   | 1015                    |      | Thr   | Asn  | Pro   | Gln<br>1020             |
| Ala | His | s Pro | о 'Туг | Phe<br>1025   |      | Glr | n Cys | Leu   | 1 Lys                   |      | n Ala | Leu  | Ala   | Thr<br>1035             |
| Asp | Asr | n His | s Val  | L Ala<br>1040 |      | Sea | c Glr | n Val | 1045                    |      | s Glu | Thr  | · Val |                         |
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ctaaattcga agcttttggt ctatattgtt aattgccatt gctgtaaatc 4150

|   |     |     |     |     |            |      |       |       |       |                         |      |     |       | •   |             |     |   | • |          |    |         |     |   |
|---|-----|-----|-----|-----|------------|------|-------|-------|-------|-------------------------|------|-----|-------|-----|-------------|-----|---|---|----------|----|---------|-----|---|
|   |     |     |     |     |            |      |       |       |       |                         |      |     |       |     |             |     |   | • |          |    |         |     |   |
|   | Asp | Phe | Lys | Gly | Leu<br>245 | Ile  | Asn   | Leu   | Thr   | Leu <sup>.</sup><br>250 | Leu  | Asp | Leu   | Ser | Gly<br>255  |     |   |   |          |    |         |     |   |
| · | Asn | Cys | Pro | Arg | Cys<br>260 | Pḥe  | Asn   | Ala   | Pro   | Phe<br>265              | Pro  | Cys | Val   | Pro | Cys<br>270  |     |   |   |          |    |         |     |   |
|   | Asp | Gly | Gly | Ala | Ser<br>275 | Ile  | Asn   | Ile   | Asp   | Arg<br>280              | Phe  | Ala | Phe   | Gln | Asn<br>285  | •   |   |   |          |    |         |     |   |
|   | Leu | Thr | Gln | Leu | Arg<br>290 | Tyr  | Leu   | Asn   | Leu   | Ser<br>295              | Ser  | Thr | Ser   | Leu | Arg<br>300  |     |   |   |          |    |         |     |   |
|   | Lys | Ile | Asn | Ala | Ala<br>305 | Trp  | Phe   | Lys   | Asn   | Met<br>310              | Pro  | His | Leu   | Lys | Val<br>315  |     |   |   | <b>'</b> |    |         |     |   |
|   | Leu | Asp | Leu | Gľu | Phe 320    | Āsnī | Tyr   | Leu   | -Val  | Gly<br>325              | Glu: | Île | Val   | Ser | Gl:y<br>330 |     |   |   | · · ·    |    | • • • • |     | - |
|   | Ala | Phe | Leu | Thr | Met<br>335 | Leu  | Pro   | Arg   | Leu   | Glu<br>340              | Ile  | Leu | Asp   | Leu | Ser<br>345  |     |   |   |          |    |         |     |   |
|   | Phe | Asn | Tyr | Ile | Lys<br>350 | Gly  | Ser   | Tyr   | Pro   | Gln<br>355              | His  | Ile | Asn   | Ile | Ser<br>360  |     |   |   |          |    |         |     |   |
|   | Arg | Asn | Phe | Ser | Lys<br>365 | Leu  | Leu   | Ser   | Leu   | Arg<br>370              | Ala  | Leu | His   | Leu | Arg<br>375  |     |   |   |          |    |         |     |   |
|   | Gly | Tyr | Val | Phe | Gln<br>380 | Glu  | Leu   | Arg   | Glu   | Asp<br>385              | Asp  | Phe | Gln   | Pro | Leu<br>390  |     |   |   |          | .• |         |     |   |
|   | Met | Gln | Leu | Pro | Asn<br>395 | Leu  | Ser   | Thr   | Ile   | Asn<br>400              | Leu  | Gly | Ile   | Asn | Phe<br>405  |     | • |   |          |    |         |     |   |
|   | Ile | Lys | Gln | Ile | Asp<br>410 | Phe  | Lys   | Leu   | Phe   | Gln<br>415              |      | Phe | Ser   | Asn | Leu<br>420  |     |   |   |          |    |         | × . |   |
|   | Glu | Ile | Ile | Tyr | Leu<br>425 |      | Glu   | Asn   | Arg   | Ile<br>430              |      | Pro | Leu   | Val | Lys<br>435  | •   |   | Ÿ |          |    |         |     |   |
|   | Asp | Thr | Arg | Gln | Ser<br>440 |      | Ala   | Asn   | Ser   | Ser<br>445              |      | Phe | Gln   |     | His<br>450  |     |   |   |          |    |         |     |   |
|   | Ile | Arg | Lys | Arg | Arg<br>455 |      | Thr   | Asp   | Pḥe   | Glu<br>460              |      | Asp | Pro   | His | Ser<br>465  |     |   |   |          |    | •       |     |   |
|   | Asn | Phe | Tyr | His | Phe<br>470 |      | Arg   | Pro   | Leu   | 11e<br>475              |      | Pro | Gln   | Cys | Ala<br>480  | . • |   |   |          |    |         |     |   |
|   | Ala | Tyr | Gly | Lys | Ala<br>485 |      | Asp   | Leu   | Ser   | 490                     |      | Ser | Ile   | Phe | Phe<br>495  |     |   |   |          |    |         |     |   |
|   | Ile | Gly | Pro | Asn | Gln<br>500 |      | e Glu | ı Asn | ı Lev | 9rc<br>505              |      | lle | : Ala | Cys | 510         |     |   |   |          | ٠  |         |     |   |
|   | Asn | Lev | Ser | Ala | Asn<br>515 |      | Asr   | Ala   | a Glr | val<br>520              |      | Ser | Gly   | Thr | Glu<br>525  |     |   |   |          |    |         |     |   |

| , |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
|---|-------------|-----|----------|---------|--------------|--------|-----------|------|------------|--------------|------|-------------|------|-------------|------------|----|---|-----|-----|---|---|-----|
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
|   |             |     | ,        |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              | •    |             |      |             |            |    |   |     |     |   |   |     |
|   | Dho         | Cor | ת ז ה    | Tla     | Pro          | шic    | Val       | Tuc  | Tur        | Lou          | ·Ven | Len         | Thr  | Aen         | Aen        |    |   |     |     |   |   |     |
| • | Pne         | Ser | AIA      | 116     | 530          | urs    | Vai       |      | ıyı        | 535          | nsp  | пец         |      | non         | 540        |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             | _    | -           |            |    | • |     |     |   |   |     |
|   | Arg         | Leu | Asp      | Phe     | Asp<br>545   | Asn    | Ala       | Ser  | Ala        | Leu<br>550   | Thr  | Glu         | Leu  | Ser         | Asp<br>555 |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
| • | Leu         | Glu | Val      | Leu     | Asp          | Leu    | Ser       | Tyr  | Asn        |              | His  | Tyr         | Phe  | Arg         |            |    |   |     |     |   |   |     |
|   |             |     |          |         | 560          |        |           |      |            | 565          |      |             |      |             | 570        |    |   |     |     |   |   |     |
|   | Ala         | Gly | Val      | Thr     | His          | His    | Leu       | Glu  | Phe        |              | Gln  | Asn         | Phe  | Thr         |            |    |   |     |     |   |   |     |
|   |             |     |          |         | 575          |        |           |      |            | 580          |      |             |      |             | 585        |    |   |     |     |   |   |     |
|   | Leu         | Lys | Val      | Leu     | Asn          | Leu    | Ser       | His  | Asn        | Asn          | Ile  | Tyr         | Thr  | Leu         | Thr        |    |   |     |     |   |   |     |
|   |             |     |          |         | 590          |        |           |      |            | 595          |      |             |      |             | 600        |    |   | ٠,  | . : |   |   |     |
|   | Asp         | Lvs | Τŷr      | Āsīn    | Leu          | Glū    | Ser       | Lvs  | Ser        | Leu          | Val  | Glu         | Leu  | -Val        | ·Phe-      |    | , |     |     |   |   |     |
|   |             | _,, | -1-      |         | 605          |        |           |      |            | 610          |      |             |      | •           | 615        |    |   |     |     |   |   |     |
|   | Com         | C1  | 7.00     | 71 ~~ ~ | Leu          | Ain    | Tla       | LOU  | Ψrn        | Δen          | Aen  | Aen         | Asn  | Δsn         | Δrα        |    |   |     |     |   |   |     |
|   | ser         | GLY | ASII     | ALG     | 620          | usp    |           | пец  | пр         | 625          | пор  | ,,op        | 1100 | 11011       | 630        |    |   |     |     |   |   |     |
|   | _           | -,  | _        | -1      | <b>D</b> 1-  | ÷      | <b>01</b> | T    | T          | 7            | T    | mb w        | 7 ~~ | T 011       | 7.00       |    |   |     |     |   | , |     |
| • | Tyr         | шe  | Ser      | тте     | Phe<br>635   | ьys    | GIY       | Leu  | гуз        | 640          | ьeu  | 1111        | Arg  | ьeu         | 645        |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        | _         |      |            | _            | _    | <b>~</b> .* |      | <b>5</b> 1. |            |    | • |     |     | • |   |     |
|   | Leu         | Ser | Leu      | Asn     | Arg<br>650   | Leu    | Lys       | His  | Ile        | Pro<br>655   |      | GIu         | Ala  | Phe         | ьеи<br>660 |    |   |     |     |   |   |     |
|   |             |     | •        |         | * :          |        |           |      |            | •            |      |             |      |             |            | ** |   | •   |     |   |   |     |
|   | Asn         | Leu | Pro      | Ala     | Ser<br>665   | Leu    | Thr       | Glu  | Leu        | His<br>670   |      | Asn         | Asp  | Asn         | Met<br>675 |    |   | .1  |     |   |   |     |
|   |             |     |          |         | 665          |        |           |      | •          | 070          |      |             | -    | ٠.          |            |    |   |     |     |   |   | . • |
|   | Leu         | Lys | Phe      | Phe     | Asn          |        | Thr       | Leu  | Leu        |              |      | Phe         | Pro  | Arg         |            |    |   | , , |     |   |   |     |
|   | •           |     |          |         | 680          |        |           |      |            | 685          |      |             |      |             | 690        |    |   |     |     | • | ٠ |     |
|   | Glu         | Leu | Leu      | Asp     | Leu          | Arg    | Gly       | Asn  | Lys        |              |      | Phe         | Leu  | Thr         |            |    |   |     |     |   |   |     |
|   |             | •   |          |         | 695          |        |           |      |            | 700          |      |             |      |             | 705        | ,  |   |     |     |   |   | .,  |
|   | Ser         | Leu | Ser      | Asp     | Phe          | Thr    | Ser       | Ser  | Leu        | Arg          | Thr  | Leu         | Leu  | Leu         | Ser        |    |   |     |     |   |   |     |
|   |             |     |          |         | 710          |        |           |      |            | 715          |      |             |      |             | 720        |    |   |     |     |   |   |     |
|   | His         | Asn | Ara      | Ile     | Ser          | His    | Leu       | Pro  | Ser        | Gly          | Phe  | Leu         | Ser  | Glu         | Val        |    |   |     |     |   |   |     |
|   |             |     | <b>J</b> |         | 725          |        |           |      |            | 730          |      |             |      |             | 735        |    |   |     |     |   |   |     |
|   | Sor         | Sar | T.e.ii   | T.ve    | His          | T.e.ii | Asn       | Len  | Ser        | Ser          | Asn  | Leu         | Leu  | Lvs         | Thr        |    |   | ,   |     |   |   |     |
|   | 561         | Jer | БСи      | נעם     | 740          |        | 1100      |      |            | 745          |      |             |      | -2,-        | 750        |    |   |     |     |   |   |     |
|   | <b>7</b> 1. | 7   | T        |         | . 71-        | T 0.1  | Ć1.,      | The  |            | ጥኮላ          | Thr  | Thr         | Luc  | Lau         | Ser        |    |   |     |     |   |   |     |
|   | iie         | ASN | гуѕ      | Ser     | 755          |        | GIU       | 1111 | . цуз      | 760          |      | 1111        | БУЗ  | пес         | 765        |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        | _         | _    | <b>5</b> 1 | <b>61</b> .  |      | m\-         |      |             | T:1 =      |    |   |     |     |   |   |     |
|   | Met         | Leu | Glu      | Lev     | 1 His<br>770 |        | Asn       | Pro  | Phe        | 775          |      | inr         | Cys  | Asp         | 780        |    |   |     |     |   | • |     |
|   |             |     |          |         |              |        |           | 31   |            |              | ť    |             |      | _           |            |    |   |     |     |   |   |     |
|   | Gly         | Asp | Phe      | Arc     | 785,         |        | Met       | Asp  | Glu        | 1 His<br>790 |      | Asn         | Val  | . Lys       | 795        |    |   |     |     |   | , |     |
|   |             |     | •        |         | •            |        |           |      | •          |              |      |             |      |             |            |    |   |     |     |   |   |     |
|   | Pro         | Arg | Leu      | ı Val   |              |        | . Ile     | Cys  | s Ala      |              |      | Gly         | Asp  | Glr         | Arg<br>810 |    |   |     |     |   |   |     |
|   |             |     |          |         | 800          |        |           |      |            | 805          |      | •           |      |             | 010        |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             | •          |    |   |     |     |   |   |     |
|   |             |     |          |         |              |        |           |      |            |              |      |             |      |             |            |    |   |     |     |   |   |     |

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Gly Lys Ser Ile Val Ser Leu Glu Leu Thr Thr Cys Val Ser Asp 820 Val Thr Ala Val Ile Leu Phe Phe Phe Thr Phe Phe Ile Thr Thr 830 835 Met Val Met Leu Ala Ala Leu Ala His His Leu Phe Tyr Trp Asp 850 Val Trp Phe Ile Tyr Asn Val Cys Leu Ala Lys Val Lys Gly Tyr 865 860 Arg Ser Leu Ser Thr Ser Gln Thr Phe Tyr Asp Ala Tyr Ile Ser 880 875 Tyr Asp Thr Lys Asp Ala Ser Val Thr Asp Trp Val-Ile Asn Glu 890 895 Leu Arg Tyr His Leu Glu Glu Ser Arg Asp Lys Asn Val Leu Leu 910 Cys Leu Glu Glu Arg Asp Trp Asp Pro Gly Leu Ala Ile Ile Asp 920 Asn Leu Met Gln Ser Ile Asn Gln Ser Lys Lys Thr Val Phe Val Leu Thr Lys Lys Tyr Ala Lys Ser Trp Asn Phe Lys Thr Ala Phe 950 955 Tyr Leu Ala Leu Gln Arg Leu Met Asp Glu Asn Met Asp Val Ile 970 965 Ile Phe Ile Leu Leu Glu Pro Val Leu Gln His Ser Gln Tyr Leu 985 Arg Leu Arg Gln Arg Ile Cys Lys Ser Ser Ile Leu Gln Trp Pro 1000 Asp Asn Pro Lys Ala Glu Gly Leu Phe Trp Gln Thr Leu Arg Asn 1010 Val Val Leu Thr Glu Asn Asp Ser Arg Tyr Asn Asn Met Tyr Val 1030 Asp Ser Ile Lys Gln Tyr <210> 499 <211> 20 <212> DNA <213> Artificial Sequence

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Gln Arg Val Tyr Gln Pro Phe Leu Thr Thr Cys Asp Gly His Arg
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Ala Cys Ser Thr Tyr Arg Thr Ile Tyr Arg Thr Ala Tyr Arg Arg

Ser Pro Gly Leu Ala Pro Ala Arg Pro Arg Tyr Ala Cys Cys Pro 80 85 90

Gly Trp Lys Arg Thr Ser Gly Leu Pro Gly Ala Cys Gly Ala Ala

Ile Cys Gln Pro Pro Cys Arg Asn Gly Gly Ser Cys Val Gln Pro 110 115 120

Gly Arg Cys Arg Cys Pro Ala Gly Trp Arg Gly Asp Thr Cys Gln

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Arg Cys Ile Asn Thr Ala Gly Ser Tyr Trp Cys Gln Cys Trp Glu

|     |     |     |     | 155        |     |     |     |     | 160        |     |     |          | •   | 165        |  |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|----------|-----|------------|--|
| Gly | His | Ser | Leu | Ser<br>170 | Ala | Asp | Gly | Thr | Leu<br>175 | Cys | Val | Pro      | Lys | Gly<br>180 |  |
| Gly | Pro | Pro | Arg | Val<br>185 | Ala | Pro | Asn | Pro | Thr<br>190 | Gly | Val | Asp      | Ser | Ala<br>195 |  |
| Met | Lys | Glu | Glu | Val<br>200 | Gln | Arg | Leu | Gln | Ser<br>205 | Arg | Val | Asp      | Leu | Leu<br>210 |  |
| Glu | Glu | Lys | Leu | Gln<br>215 | Leu | Val | Leu | Ala | Pro<br>220 | Leu | His | Ser      | Leu | Ala<br>225 |  |
| Ser | Gln | Ala | Leu | Glu<br>230 | His | Gly | Leu | Pro | Asp<br>235 | Pro | Gly | Ser      | Leu | Leu<br>240 |  |
| Val | His | Ser | Phe | Gln<br>245 | Gln | Leu | Gly | Arg | Ile<br>250 | Asp | Ser | Leu<br>, | Ser | Glu<br>255 |  |
| Gln | Ile | Ser | Phe | Leu        | Glu | Glu | Gln | Leu | Gly        | Ser | Cys | Ser      | Cys | Lys        |  |

265

Lys Asp Ser

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Cys Ala Val Arg Ala His Gly Asp Pro Val Ser Glu Ser Phe Val

<sup>&</sup>lt;210> 508

<sup>&</sup>lt;211> 273

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

| Gln  | Arg          | Val   | Tyr  | Gln<br>50  | Pro | Phe | Leu | Thr | Thr.        | Cys | Asp | GIY  | His  | Arg<br>60   |
|------|--------------|-------|------|------------|-----|-----|-----|-----|-------------|-----|-----|------|------|-------------|
| Ala  | Cys          | Ser   | Thr  | Tyr<br>65  | Arg | Thr | Ile | Tyr | Arg<br>70   | Thr | Ala | Tyr  | Arg  | Arg<br>75   |
| Ser  | Pro          | Gly   | Leu  | Ala<br>80  | Pro | Ala | Arg | Pro | Arg<br>85   | Tyr | Ala | Cys  | Cys  | Pro<br>90   |
| Gly  | Trp          | Lys   | Arg  | Thr<br>95  | Ser | Gly | Leu | Pro | Gly.<br>100 | Ala | Cys | Gly  | Ala  | Ala<br>105  |
| Ile  | Cys          | Gln   | Pro  | Pro<br>110 | Cys | Arg | Asn | Gly | Gly<br>115  | Ser | Cys | Val  | Gln  | Pro<br>120  |
| Gly  | Arg          | Су́s  | Ārg  | Cÿs<br>125 | Pro | Ala | Gly | Trp | Arg<br>130  | Gly | Asp | -Thr | -Cys | Gln-<br>135 |
| Ser  | Asp          | Val   | Asp  | Glu<br>140 | Cys | Ser | Ala | Arg | Arg<br>145  | Gly | Gly | Cys  | Pro  | Gln<br>150  |
| Arg  | Cys          | Ile   | Asn  | Thr<br>155 | Ala | Gly | Ser | Tyr | Trp<br>160  | Cys | Gln | Cys  | Trp  | Glu<br>165  |
| Gly  | His          | Ser   | Leu  | Ser<br>170 | Ala | Asp | Gly | Thr | Leu<br>175  | Cys | Val | Pro  | Lys  | Gly<br>18.0 |
| Gly  | Pro          | Pro   | Arg  | Val<br>185 | Ala | Pro | Asn | Pro | Thr<br>190  | Gly | Val | Asp  | Ser  | Ala<br>195  |
| Met  | Lys          | Glu   | Glu  | Val<br>200 | Gln | Arg | Leu | Gln | Ser<br>205  | Arg | Val | Asp  | Leu  | Leu<br>210  |
| Glu  | Glu          | . Lys | Leu  | Gln<br>215 | Leu | Val | Leu | Ala | Pro<br>220  | Leu | His | Ser  | Leu  | Ala<br>225  |
| Ser  | Gln          | Ala   | Leu  | Glu<br>230 | His | Gly | Leu | Pro | Asp<br>235  | Pro | Gly | Ser  | Leu  | Leu<br>240  |
| Val  | His          | Ser   | Phe  | Gln<br>245 | Gln | Leu | Gly | Arg | Ile<br>250  |     | Ser | Leu  | Ser  | Glu<br>255  |
| Gln  | Ile          | Ser   | Phe  | Leu<br>260 |     | Glu | Gln | Leu | Gly<br>265  |     | Cys | Ser  | Cys  | Lys<br>270  |
| Lys  | Asp          | Ser   |      |            |     |     |     |     |             |     |     |      |      |             |
| <211 | > 50<br>> 15 | 38    |      |            |     |     |     |     |             |     |     |      |      |             |
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|--|---------------------------------|
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| Ala Wal Cly Cly Thr Cly His Ala Tyr Arg Pro Gly Arg A  | 30 Phe Val45 His Arg            |
| 20 25  | 45_<br>His Arg                  |
| Cys Ala Val Arg Ala His Gly Asp Pro Val Ser Glu Ser I  |                                 |
| Gln Arg Val Tyr Gln Pro Phe Leu Thr Thr Cys Asp Gly F<br>50 55   | 00                              |
| Ala Cys Ser Thr Tyr Arg Thr Ile Tyr Arg Thr Ala Tyr A  | Arg Arg<br>75                   |
| Ser Pro Gly Leu Ala Pro Ala Arg Pro Arg Tyr Ala Cys (  | Cys Pro<br>90                   |
| Gly Trp Lys Arg Thr Ser Gly Leu Pro Gly Ala Cys Gly 7 95 100   | Ala Ala<br>105                  |
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| Gly Arg Cys Arg Cys Pro Ala Gly Trp Arg Gly Asp Thr  | Cys Gln<br>135                  |
| Ser Asp Val Asp Glu Cys Ser Ala Arg Arg Gly Gly Cys<br>140 145   | Pro Gln<br>150                  |
| Arg Cys Val Asn Thr Ala Gly Ser Tyr Trp Cys Gln Cys<br>155 160   | Trp Glu<br>165                  |
| Gly His Ser Leu Ser Ala Asp Gly Thr Leu Cys Val Pro<br>170 175   | Lys Gly<br>180                  |
| Gly Pro Pro Arg Val Ala Pro Asn Pro Thr Gly Val Asp<br>185 190   | Ser Ala<br>195                  |
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| Glu Glu Lys Leu Gln Leu Val Leu Ala Pro Leu His Ser<br>215 220   | Leu Ala<br>225                  |
| Ser Gln Ala Leu Glu His Gly Leu Pro Asp Pro Gly Ser 230 235  | Leu Leu<br>240                  |

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<211> 364

<212> PRT

<213> Homo sapiens

<400> 515

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Lys Leu Pro Gly Arg Asn Thr Phe Cys Cys Asp Gly Arg Val Met

25.

|          |     |     |     | ,          |     |      |     |     |            |     | •   |          |          |             |
|----------|-----|-----|-----|------------|-----|------|-----|-----|------------|-----|-----|----------|----------|-------------|
| Met      | Ala | Arg | Gln | Lys<br>35  | Gly | Ile  | Phe | Tyr | Leu<br>40  | Thr | Leu | Phe      | Leu      | Ile<br>45   |
| Leu      | Gly | Thr | Cys | Thr<br>50  | Leu | Phe  | Phe | Ala | Phe<br>55  | Glu | Cys | Arg      | Tyr      | Leu<br>60 . |
| Ala      | Val | Gln | Leu | Ser<br>65  | Pro | Ala  | Ile | Pro | Val<br>70  | Phe | Àla | Ala      | Met      | Leu<br>75   |
| Phe      | Leu | Phe | Ser | Met<br>80  | Ala | Thr  | Leu | Leu | Arg<br>85  | Thr | Ser | Phe      | Ser      | Asp<br>90   |
| Pro      | Gly | Val | Ile | Pro<br>95  | Arg | Ala  | Leu | Pro | Asp<br>100 | Glu | Ala | Ala      | Phe      | Ile<br>105  |
| Glu      | Met | Glu | Ile | Glu<br>110 | Ala | Thr  | Asn | Gly | Ala<br>115 | Val | Pro | Gln      | Gly      | Gĺn<br>120  |
| Arg      | Pro | Pro | Pro | Arg<br>125 | Ile | Lys  | Asn | Phe | Gln<br>130 | Ile | Asn | Asn      | Gln      | Ile<br>135  |
| Val<br>, | Lys | Leu | Lys | Tyr<br>140 | Cys | Tyr  | Thr | Cys | Lys<br>145 | Ile | Phe | Arg      | Pro      | Pro<br>150  |
| Arg      | Ala | Ser | His | Cys<br>155 | Ser | Ile  | Cys | Asp | Asn<br>160 | Cys | Val | Glu      | Arg      | Phe<br>165  |
| Asp      | His | His | Cys | Pro<br>170 | Trp | Val  | Gly | Asn | Cys<br>175 | Val | Gly | Lys      | Arg      | Asn<br>180  |
| Tyr      | Arg | Tyr | Phe | Tyr<br>185 | Leu | Phe  | Ile | Leu | Ser<br>190 | Leu | Ser | Leu      | Leu<br>· | Thr<br>195  |
| Ile      | Tyr | Val | Phe | Ala<br>200 | Phe | Asn  | Ile | Val | Tyr<br>205 | Val | Ala | Leu      | Lys      | Ser<br>210  |
| Leu      | Lys | Ile | Gly | Phe<br>215 |     | Glu  | Thr | Leu | Lys<br>220 | Glu | Thr | Pro      | Ġly      | Thr<br>225  |
| Val      | Leu | Glu | Val | Leu<br>230 | Ile | Cys  | Phe | Phe | Thr<br>235 | Leu | Trp | Ser      | Val      | Val<br>240  |
| Gly      | Leu | Thr | Gly | Phe<br>245 |     | Thr  | Phe | Leu | Val<br>250 | Ala | Leu | Asn      | Gln      | Thr<br>255  |
| Thr      | Asn | Glu | Asp | Ile<br>260 |     | Gly  | Ser | Trp | Thr<br>265 | Gly | Lys | Asn      | Arg      | Val.<br>270 |
| Gln      | Asn | Pro | Tyr | Ser<br>275 |     | .Gly | Asn | Ile | Val<br>280 |     | Asn | Cys<br>, | Суз      | Glu<br>285  |
| Val      | Leu | Cys | Gly | Pro<br>290 |     | Pro  | Pro | Ser | Val<br>295 | Leu | Asp | Arg      | Arg      | Gly<br>300  |
| Ile      | Leu | Pro | Leu | Glu        | Glu | Ser  | Gly | Ser | Arg        | Pro | Pro | Ser      | Thr      | Gln         |

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<400> 516

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<sup>&</sup>lt;210> 523 ...

<sup>&</sup>lt;211> 344

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

|            |         | 523 |     |      |            | _   | _                |     | •     | _          | _   |     | _     | _     | _ •        |
|------------|---------|-----|-----|------|------------|-----|------------------|-----|-------|------------|-----|-----|-------|-------|------------|
| M          | et<br>1 | Lys | Thr | Ile  | Gln<br>5   | Pro | Lys              | Met | His   | Asn 10     | Ser | Ile | Ser   | Trp   | Ala<br>15  |
| I          | le      | Phe | Thr | Gly  | Leu<br>20  | Ala | Ala <sub>.</sub> | Leu | Cys   | Leu<br>25  | Phe | Gln | Gly   | Val   | Pro<br>30  |
| V          | al      | Arg | Ser | Gly  | Asp<br>35  | Ala | Thr              | Phe | Pro   | Lys<br>40  | Ala | Met | Asp   | Asn   | Val<br>45  |
| Т          | hr      | Val | Arg | Gln  | Gly<br>50  | Glu | Ser              | Ala | Thr   | Leu<br>55  | Arg | Cys | Thr   | Ile   | Asp<br>60  |
| A          | sn      | Arg | Val | Thr  | Arg<br>65  | Val | Ala              | Trp | Leu   | Asn<br>70  | Arg | Ser | Thr   | Ile   | Leu<br>75  |
| · - T      | yr      | Ala | Gly | Asn- | Asp<br>80  | Lys | -Trp             | Cys | . Leu | Asp<br>85  | Pro | Arg | _Val  | Val.  | Leu<br>90  |
| L          | eu      | Ser | Asn | Thr  | Gln<br>95  | Thr | Gln              | Tyr | Ser   | Ile<br>100 | Glu | Ile | Gln   | Asn   | Val<br>105 |
| A          | .sp     | Val | Tyr | Asp  | Glu<br>110 | Gly | Pro              | Tyr | Thr   | Cys<br>115 | Ser | Val | Gln   | Thr   | Asp<br>120 |
| . <b>A</b> | sn      | His | Pro | Lys  | Thr<br>125 | Ser | Arg              | Val | His   | Leu<br>130 | Ile | Val | Gln   | Val   | Ser<br>135 |
| · F        | ro      | Lys | Ile | Val  | Glu<br>140 | Ile | Ser              | Ser | Asp   | Ile<br>145 | Ser | Ile | Asn   | Glu   | Gly<br>150 |
| P          | sn      | Asn | Ile | Ser  | Leu<br>155 | Thr | Cys              | Ile | Ala   | Thr<br>160 | Gly | Arg | Pro   | Glu   | Pro<br>165 |
| T          | hr      | Val | Thr | Trp  | Arg<br>170 |     | Ile              | Ser | Pro   | Lys<br>175 | Ala | Val | Gly   | Phe   | Val<br>180 |
| S          | Ser     | Glu | Asp | Glu  | Tyr<br>185 | Leu | Glu              | Ile | Gln   | Gly<br>190 |     | Thr | Arg   | Glu   | Gln<br>195 |
| S          | Ser     | Gly | Asp | Tyr  | Glu<br>200 | Cys | Ser              | Ala | Ser   | Asn<br>205 |     | Val | Ala   | Ala   | Pro<br>210 |
| 7          | /al     | Val | Arg | Arg  | Val<br>215 | Lys | Val              | Thr | .Val  | Asn<br>220 |     | Pro | Pro   | Tyr   | Ile<br>225 |
| 5          | Ser     | Glu | Ala | Lys  | Gly<br>230 | Thr | Gly              | Val | Pro   | Val<br>235 |     | Gln | Lys   | Gly   | Thr<br>240 |
| 1          | Leu     | Gln | Cys | Glu  | Ala<br>245 | Ser | Ala              | Val | Pro   | Ser<br>250 |     | Glu | . Phe | Gln   | Trp<br>255 |
|            | ſyr     | Lys | Asp | Asp  | Lys<br>260 | Arg | Leu              | Ile | Glu   | Gly<br>265 |     | Lys | Gly   | Val   | Lys<br>270 |
| 1          | Val     | Glu | Asn | Arg  | Pro<br>275 | Phe | Leu              | Ser | Lys   | Leu<br>280 |     | Phe | Phe   | . Asn | Val<br>285 |

d .

Ser Glu His Asp Tyr Gly Asn Tyr Thr Cys Val Ala Ser Asn Lys Leu Gly His Thr Asn Ala Ser Ile Met Leu Phe Gly Pro Gly Ala 305 310 Val Ser Glu Val Ser Asn Gly Thr Ser Arg Arg Ala Gly Cys Val Trp Leu Leu Pro Leu Leu Val Leu His Leu Leu Leu Lys Phe <210> 524 <211> 503 <212> DNA <213> Homo sapiens <400> 524 gaaaaaaaat catgaaaacc atccagccaa aaatgcacaa ttctatctct 50 tgggcaatct tcacggggct ggctgctctg tgtctcttcc aaggagtgcc 100 cgtgcgcagc ggagatgcca ccttccccaa agctatggac aacgtgacgg 150 tccggcaggg ggagagcgcc accctcaggt gcactattga caaccgggtc 200 accogggtgg cotggctaaa cogcagcaco atcototatg ctgggaatga 250 caagtggtgc ctggatcctc gcgtggtcct tctgagcaac acccaaacgc 300 agtacagcat cgagatccag aacgtggatg tgtatgacga gggcccttac 350 acctgctcgg tgcagacaga caaccaccca aagacctcta gggtccacct 400 cattgtgcaa gtatctccca aaattgtaga gatttcttca gatatctcca 450 ttaatgaagg gaacaatatt agcctcacct gcatagcaac tggtagacca 500 gag 503 <210> 525 <211> 2602 "

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35 40 45

Leu Gly Cys Leu Val Ala Leu Gly Val Gln Tyr His Arg Asp Pro
50 55 60

|      | Ser | His | Ser | Thr   | Cys<br>65   | Leu      | Thr | Glu | Ala   | Cys<br>70  | Ile | Arg | Val  | Ala | Gly<br>75   |
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|      | Lys | Ile | Leu | Glu   | Ser<br>80   | Leu      | Asp | Arg | Gly   | Val<br>85  | Ser | Pro | Cys  | Glu | Asp<br>90   |
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|      | Asn | Ser | Ser |       |             |          | Glu |     |       |            |     |     |      |     | Leu<br>150- |
| α.   | Ser | Cys | Leu | Gln   | Val<br>155  | Glu      | Arg | Ile | Glu   | Glu<br>160 | Leu | Gly | Ala  | Gln | Pro<br>165  |
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|      | Pro | Trp | Asp |       | Asp<br>,185 | Asn      | Phe | Met | Glu   | Val<br>190 | Leu | Lys | Ala  | Val | Ala<br>195  |
|      | Gly | Thr | Tyr | Arg   | Ala<br>200  | Thr      | Pro | Phe | Phe   | Thr<br>205 | Val | Tyr | Ile  | Ser | Ala<br>210  |
| •    | Asp | Ser | Lys | Ser   | Ser<br>215  | Asn      | Ser | Asn | Val   | Ile<br>220 | Gln | Val | Asp  | Gln | Ser<br>225  |
|      | Gly | Leu | Phe | Leu   | Pro<br>230  | Ser<br>' | Arg | Ąsp | Tyr   | Tyr<br>235 | Leu | Asn | Arg  | Thr | Ala<br>240  |
|      | Asn | Glu | Lys | Val   | Leu<br>245  | Thr      | Ala | Tyr | Leu   | Asp<br>250 | Tyr | Met | Glu  | Glu | Leu<br>255  |
|      | Gly | Met | Leu | Leu   | Gly<br>260  |          | Arg | Pro | Thr   | Ser<br>265 | Thr | Arg | `Glu | Gln | Met<br>270  |
| - 10 | Gln | Gln | Val | Leu   | Glu<br>275  |          | Glu | Ile | Gln   | Leu<br>280 |     | Asn | Ile  | Thr | Val<br>285  |
|      | Pro | Gln | Asp | Gln   | Arg<br>290  |          | Asp | Glu | Glu   | Lys<br>295 |     | Tyr | His  | Lys | Met<br>300  |
|      | Ser | Ile | Ser | Glu   | Leu<br>305  |          | Ala | Leu | Ala   | Pro<br>310 |     | Met | Asp  | Trp | Leu<br>315  |
|      | Glu | Phe | Leu | Ser   | Phe<br>320  |          | Leu | Ser | Pro   | Leu<br>325 |     | Leu | Ser  | Asp | Ser<br>330  |
|      | Glu | Pro | Val | . Val | Val<br>335  | i        | Gly | Met | : Asp | 340        |     | Gln | Glr  | Val | Ser<br>345  |
|      |     |     |     |       |             | )<br>')  |     |     |       |            |     |     |      |     |             |

|     | Glu | Leu | Ile  | Asn  | Arg<br>350 | Thr | Glu | Pro | Ser   | Ile<br>355  |     | Asn | Asn | Tyr   | Leu<br>360  | ,   |   |   |    |   |  |
|-----|-----|-----|------|------|------------|-----|-----|-----|-------|-------------|-----|-----|-----|-------|-------------|-----|---|---|----|---|--|
|     | Ile | Trp | Asn  | Leu  | Val<br>365 | Gln | Lys | Thr | Thr   | Ser<br>370  | Ser | Leu | Asp | Ârg   | Arg<br>375  |     |   |   |    |   |  |
| · . | Phe | Glu | Ser  | Ala  | Gln<br>380 | Glu | Lys | Leu | Leu   | Glu<br>385  | Thr | Leu | Tyr | Gly   | Thr<br>390  |     | • |   |    |   |  |
|     | Lys | Lys | Ser  | Cys, | Val<br>395 | Pro | Arg | Trp | Gln   | Thr<br>400  |     | Ile | Ser | Asn   | Thr<br>405  |     |   |   |    |   |  |
|     | Asp | Asp | Ala  | Leu  | Gly<br>410 | Phe | Ala | Leu | Gly   | Ser<br>415  | Leu | Phe | Val | Lys   | Ala<br>420  |     |   |   |    |   |  |
|     | Thr | Phe |      |      |            |     | Lys |     |       |             |     |     |     |       | Ser<br>435. |     | , |   | 3  |   |  |
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|     | Ile | Tyr | Asp  | Met  | Ile<br>470 | Gly | Phe | Pro | Asp   | Phe<br>475  | Ile | Leu | Glu | Pro   | Lys<br>480  | , . |   |   |    |   |  |
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| · · | Phe | Phe | Gln  | Asn  | Met<br>500 | Leu | Asn | Leu | Tyr   | Asn<br>505  |     | Ser | Ala | Lys   | Val<br>510  |     |   |   |    |   |  |
|     | Met | Ala | Asp  | Gln  | Leu<br>515 | Arg | Lys | Pro | Pro   | Ser<br>520  | Arg | Asp | Gln | Trp   | Ser<br>525  | • ` |   |   |    |   |  |
|     | Met | Thr | Pro  | Gln  | Thr<br>530 |     | Asn | Ala | Tyr   | Tyr<br>535  |     | Pro | Thr | Lys   | Asn<br>540  | ,   |   | • |    |   |  |
|     | Glu | Ile | Val  | Phe  | Pro<br>545 | Ala | Gly | Ile | Leu   | Gln<br>550  |     | Pro | Phe | Tyr   | Ala<br>555  |     |   |   |    | , |  |
|     | Arg | Asn | His  | Pro  | Lys<br>560 |     | Leu | Asn | Phe   | Gly<br>565  |     | Ile | Gly | Val   | Val<br>570  |     |   |   |    |   |  |
| ·   | Met | Gly | His  | Glu  | Leu<br>575 | Thr | His | Ala | Phe   | Asp<br>580  | -   | Gln | Gly | Arg   | Glu<br>585  |     |   |   |    |   |  |
|     | Tyr | Asp | Lys  | Glu  | Gly<br>590 |     | Leu | Arg | Pro   | Trp<br>595  | _   | Gln | Asn | Glu   | Ser<br>600  |     |   |   | ٠. |   |  |
| * . | Leu | Ala | Ala  | Phe  | Arg<br>605 |     | His | Thr | · Ala | Cys<br>610  |     | Glu | Glu | Gln   | Tyr<br>615  |     |   |   |    |   |  |
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Leu Gly Glu Asn Ile Thr Asp Asn Gly Gly Leu Lys Ala Ala Tyr Asn Ala Tyr Lys Ala Trp Leu Arg Lys His Gly Glu Glu Gln Gln Leu Pro Ala Val Gly Leu Thr Asn His Gln Leu Phe Phe Val Gly 665 670 Phe Ala Gln Val Trp Cys Ser Val Arg Thr Pro Glu Ser Ser His 680 Glu Gly Leu Val Thr Asp Pro His Ser Pro Ala Arg Phe Arg Val 695 Leu Gly Thr Leu Ser Asn Ser Arg Asp Phe Leu Arg His Phe Gly 720 Cys Pro Val Gly Ser Pro Met Asn Pro Gly Gln Leu Cys Glu Val 725 Trp <210> 527 <211> 4308 <212> DNA <213> Homo sapiens <220> <221> unsure <222> 1478, 3978, 4057-4058, 4070 <223> unknown base

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Pro Ala Gly Gln Ser Val Asp Phe Pro Trp Ala Ala Val Asp Asn
40
45

Met Met Val Arg Lys Gly Asp Thr Ala Val Leu Arg Cys Tyr Leu 50 55 60

Glu Asp Gly Ala Ser Lys Gly Ala Trp Leu Asn Arg Ser Ser Ile 65 70 75

Ile Phe Ala Gly Gly Asp Lys Trp Ser Val Asp Pro Arg Val Ser 80 85 90

Ile Ser Thr Leu Asn Lys Arg Asp Tyr Ser Leu Gln Ile Gln Asn 95 100 105

Val Asp Val Thr Asp Asp Gly Pro Tyr Thr Cys Ser Val Gln Thr

<sup>&</sup>lt;211> 352

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo Sapien

|      |              |     |       |            |       |       |       |       | •          |       |       |      |      |            |
|------|--------------|-----|-------|------------|-------|-------|-------|-------|------------|-------|-------|------|------|------------|
|      |              |     |       | 110        |       |       |       |       | 115        |       |       |      |      | 120        |
| Gln  | His          | Thr | Pro   | Arg<br>125 | Thr   | Met   | Gln   | Val   | His<br>130 | Leu   | Thr   | Val  | Gln  | Val<br>135 |
| Pro  | Pro          | Lys | Ile   | Tyr<br>140 | Asp   | Ile   | Ser   | Asn   | Asp<br>145 | Met   | Thr   | Vaļ  | Asn  | Glu<br>150 |
| Gly  | Thr          | Asn | Val   | Thr<br>155 | Leu   | Thr   | Cys   | Leu   | Ala<br>160 | Thr   | Gly   | Lys  | Pro  | Glu<br>165 |
| Pro  | Ser<br>      | Ile | Ser   | Trp<br>170 | Arg   | His   | Ile   | Ser   | Pro<br>175 | Ser   | Ala   | Lys  | Pro  | Phe<br>180 |
| Glu  | Asn          | Gly | Gln   | Tyr<br>185 | Leu   | Asp   | Ile   | Tyr   | Gly<br>190 | Ile   | Thr   | Arg  | Asp  | Gln<br>195 |
| Ālā  | Gly          | Glu | Tyr   | Glü<br>200 | Cys   | Ser   | Ala   | Glu   | Asn<br>205 | -Ala- | Val-  | Ser  | Phe  | Pro-       |
| Asp  | Val          | Arg | Lys   | Val<br>215 | Lys   | Val   | Val   | Val   | Asn<br>220 | Phe   | Ala   | Pro  | Thr  | Ile<br>225 |
| Gln  | Glu          | Ile | Lys   | Ser<br>230 | Gly   | Thr   | Val   | Thr   | Pro<br>235 | Gly   | Arg   | Ser  | Gly  | Leu<br>240 |
| Ile  | Arg          | Cys | Glu   | Gly<br>245 | Ala   | Gly   | Val   | Pro   | Pro<br>250 | Pro   | Ala   | Phe  | Glu  | Trp<br>255 |
| Tyr  | Lys          | Gly | Glu   | Lys<br>260 |       | Leu   | Phe   | Asn   | Gly<br>265 | Gln   | Gln   | Gly  | Ile  | Ile<br>270 |
| Ile  | Gln          | Asn | Phe   | Ser<br>275 | Tḥr   | Arg   | Ser   | Ile   | Leu<br>280 | Thr   | Val   | Thr  | Asn  | Val<br>285 |
| Thr  | Gln          | Glu | His   | Phe<br>290 |       | Asn   | Tyr   | Thr   | Cys<br>295 | Val   | Ala   | Ala  | Asn  | Lys<br>300 |
| Leu  | Gly          | Thr | Thr   | Asn<br>305 |       | Ser   | Leu   | Pro   | Leu<br>310 | Asn   | Pro   | Pro  | Ser  | Thr<br>315 |
| Ala  | Gln          | Tyr | Gly   | Ile<br>320 |       | Gly   | Ser   | Ala   | Asp<br>325 | Val   | Leu   | Phe  | Ser  | Cys<br>330 |
| Trp  | Tyr          | Leu | Val   | Leu<br>335 |       | Leu   | Ser   | Ser   | Phe<br>340 |       | Ser   | Ile  | Phe  | Tyr<br>345 |
| Leu  | Lys          | Asn | Ala   | Ile<br>350 |       | Gln   | 1     |       |            |       |       |      |      |            |
| <212 | > 17<br>> DN | 97  | Sapie | en         |       |       |       |       |            | •     |       |      |      |            |
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<211> 520

<212> PRT

<213> Homo Sapien

<400> 614

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Thr Gln Gln Ala Ala Phe His Gln Ile Ala Met Glu Pro Phe Glu 20 25 30

Ile Asn Val Pro Lys Pro Lys Arg Arg Asn Gly Val Asn Phe Ser 35 40 45

Leu Ala Val Val Ile Tyr Leu Ile Leu Leu Thr Ala Gly Ala 50 55 60

Gly Leu Leu Val Val Gln Val Leu Asn Leu Gln Ala Arg Leu Arg
65 70 75

Val Leu Glu Met Tyr Phe Leu Asn Asp Thr Leu Ala Ala Glu Asp 80 85 90

Ser Pro Ser Phe Ser Leu Leu Gln Ser Ala His Pro Gly Glu His
95 100 105

Leu Ala Gln Gly Ala Ser Arg Leu Gln Val Leu Gln Ala Gln Leu
110 115 120

Thr Trp Val Arg Val Ser His Glu His Leu Leu Gln Arg Val Asp 125 130 135

Asn Phe Thr Gln Asn Pro Gly Met Phe Arg Ile Lys Gly Glu Gln 140 145 150

Gly Ala Pro Gly Leu Gln Gly His Lys Gly Ala Met Gly Met Pro

Gly Ala Pro Gly Pro Gly Pro Pro Ala Glu Lys Gly Ala Lys

Gly Ala Met Gly Arg Asp Gly Ala Thr Gly Pro Ser Gly Pro Gln

|   | ,   |     |       |      |            |      |       |       |        |              |       |       |       |     |            |
|---|-----|-----|-------|------|------------|------|-------|-------|--------|--------------|-------|-------|-------|-----|------------|
|   | Gly | Pro | Pro   | Gly  | Val<br>200 | Ĺys  | Gly   | Glu   | Ala    | Gly<br>205   | Leu   | Gln   | Gly   | Pro | Gln<br>210 |
|   | Gly | Ala | Pro   | Gly  | Lys<br>215 | Gln  | Gly   | Ala   | Thr    | Gly<br>220   | Thr   | Pro   | Gly   | Pro | Gln<br>225 |
| , | Gly | Glu | Lys   | Gly  | Ser<br>230 | Lys  | Gly   | Asp   | Gly    | Gly<br>235   | Leu   | Ile   | Gly   | Pro | Lys<br>240 |
|   | Gľy | Glu | Thr   | Gly  | Thr<br>245 | Lys  | Gly   | Glu   | Lys    | Gly<br>250   | Asp   | Leu   | Gly   | Leu | Pro<br>255 |
| , | Gly | Ser | Lys   | Gly  | Asp<br>260 | Arg  | Gly   | Met   | Lys    | Gly<br>265   | Asp   | Ala   | Gly   | Val | Met<br>270 |
| - | Gly | Pro | Pro   | Gly  | Ala<br>275 | -Gln | Gly   | Ser   | Lys    | Gly<br>280   | Asp   | Phe   | Gly   |     | Pro<br>285 |
|   | Gly | Pro | Pro   | Ġly  | Leu<br>290 | Ala  | Gly   | Phe   | Pro    | Gly<br>295   | Ala   | Lys   | Gly   | Asp | Gln<br>300 |
|   | Gly | Ģln | Pro   | Gly  | Leu<br>305 | Gln  | Gly   | Val   | Pro    | Gly<br>310   | Pro   | Pro   | Gly   | Ala | Val<br>315 |
|   | Gly | His | Pro   | Gly  | Ala<br>320 | Lys  | Gly   | Glu   | Pro    | Gly<br>325   | Ser   | Ala   | Gly   | Ser | Pro<br>330 |
|   | Gly | Arg | Ala   | Gly  | Leu<br>335 | Pro  | Gly   | Ser   | Pro    | Gly<br>340   | Ser   | Pro   | Gly   | Ala | Thr<br>345 |
|   | Gly | Leu | Lys   | Gly  | Ser<br>350 |      | Gly   | Asp   | Thr    | Gly<br>355   |       | Gln   | Gly   | Gln | Gln<br>360 |
|   | Gly | Arg | Lys   | Gly  | Glu<br>365 |      | Gly   | Val   | Pro    | Gly<br>370   |       | Ala   | Gly   | Val | Lys<br>375 |
|   | Gly | Glu | Gln   | Gly  | Ser<br>380 |      | Gly   | Leu   | Ala    | Gly<br>385   | Pro   | Lys   | Gly   | Ala | Pro<br>390 |
|   | Gly | Gln | Ala   | Gly  | Gln<br>395 |      | Gly   | Asp   | Gln    | Gly<br>400   |       | Lys   | Gly   | Ser | Ser<br>405 |
|   | Gly | Glu | Gln   | Gly  | Val<br>410 |      | Gly   | Glu   | Lys    | Gly<br>415   |       | Arg   | Gly   | Glu | Asn<br>420 |
|   | Ser | Val | Ser   | Val  | Arg<br>425 |      | Val   | Gly   | Ser    | Ser<br>430   |       | Arg   | Gly   | Arg | Ala<br>435 |
|   | Glu | Val | Туг   | Tyr  | Ser<br>440 |      | , Thr | Trp   | Gly    | 7 Thr<br>445 |       | . Cys | Asp   | Asp | Glu<br>450 |
|   | Trp | Glr | Asr   | Ser  | 455        |      | Īle   | e Val | Phe    | Cys<br>460   |       | , Met | Leu   | Gly | Tyr<br>465 |
|   | 0   |     | . 61. | . 70 | . 77 -     |      | . m.  | . T   | . 17-1 | C1.          | . 71. |       | · mh~ | C1. | , Cln      |

Ile Trp Leu Asp Asn Val Gln Cys Arg Gly Thr Glu Ser Thr Leu 485 490 495

Trp Ser Cys Thr Lys Asn Ser Trp Gly His His Asp Cys Ser His 500 505 510

Glu Glu Asp Ala Gly Val Glu Cys Ser Val 515 520

<210> 615

<211> 647

<212> DNA

<213> Homo Sapien

<400> 615

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<210> 616

<211> 98

<212> PRT

<213> Homo Sapien ·

<400> 616

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Lys Ile Leu Lys Asp His Asn Cys His Asn Leu Pro Glu Gly Val

Ala Asp Leu Thr Gln Ile Asp Val Asn Val Gln Asp His Phe Trp
50 55 60

Asp Gly Lys Gly Cys Glu Met Ile Cys Tyr Cys Asn Phe Ser Glu 65 70 75

Leu Leu Cys Cys Pro Lys Asp Val Phe Phe Gly Pro Lys Ile Ser 80 85 90

Phe Val Ile Pro Cys Asn Asn Gln 95

<210> 617

<211> 2558

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<213> Homo Sapien

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|---|------------|------|------|------------|------|------|------|-----|------------|-----|------|------|------|------------|
| gtat  | attg       | at a | aatt | ttaa       | a at | tggt | atat | ttg | aaaț       | aaa | gttg | aata | tt 2 | 550        |
| atat  | ataa       | 255  | 8    |            |      |      | •    |     |            |     |      | -    |      | •          |
| <210><211><211><212><213>                                   | 750<br>PRT |      | pien |            |      | . 1  |      |     |            |     |      |      | •    |            |
| <400>   |            |      |      |            |      |      |      |     |            | ,   |      |      |      |            |
| Met<br>1  | Trp        | Asn  | Leu  | Leu<br>5   | His  |      |      |     | Ser<br>10  | Ala | Val  | Ala  | Thr  | A1a<br>15  |
| Arg   | <br>Arg    | Pro  | Arg  | Trp<br>20  | Leu  | Cys  | Ala  |     | Ala<br>25  | Leu | Val  | Leu  | Ala  | Gly<br>30  |
| Gly   | Phe        | Phe  | Leu  | Leu<br>35  | Gly  | Phe  | Leu  | Phe | Gly<br>40  | Trp | Phe  | Ile  | Lys  | Ser<br>45  |
| Ser   | Asn        | Glu  | Ala  | Thr<br>50  | Asn  | Ile  | Thr  | Pro | Lys<br>55  | His | Asn  | Met  | Lys  | Ala<br>60  |
| Phe   | Leu        | Asp  | Glu  | Leu<br>65  | Lys  | Ala  | Glu  | Asn | Ile<br>70  | Lys | Lys  | Phe  | Leu  | His<br>75  |
| Asn   | Phe        | Thr  | Gln  | Ile<br>80  | Pro  | His  | Leu  | Ala | Gly<br>85  | Thr | Glu  | Gln  | Asn  | Phe<br>90  |
| Gln   | Leu        | Ala  | Lys  | Gln<br>95  | Ile  | Gln  | Ser  | Gln | Trp<br>100 | Lys | Glu  | Phe  | Gly  | Leu<br>105 |
| Asp   | Ser        | Val  | Glu  | Leu<br>110 | Ala  | His  | Tyr  | Ÿsp | Val<br>115 | Leu | Leu  | Ser  | Tyr  | Pro<br>120 |
| Asn   | Lys        | Thr  | His  | Pro<br>125 | Asn  | Tyr  | Ile  | Ser | Ile<br>130 | Iľe | Asn  | Glu  | Asp  | Gly<br>135 |
| Asn   | Glu        | Ile  | Phe  | Asn<br>140 | Thr  | Ser  | Leu  | Phe | Glu<br>145 | Pro | Pro  | Pro  | Pro  | Gly<br>150 |
| Tyr   | Glu        | Asn  | Val  | Ser<br>155 | Asp  | Ile  | Val  | Pro | Pro<br>160 | Phe | Ser  | Ala  | Phe  | Ser<br>165 |
| Pro   | Gln        | Gly  | Met  | Pro<br>170 |      | Gly  | Asp  | Leu | Val<br>175 | Tyr | Val  | Asn  | Tyr  | Ala<br>180 |
| Arg   | Thr        | Glu  | Asp  | Phe<br>185 |      | Lys  | Leu  | Glu | Arg<br>190 | Asp | Met  | Lys  | Ile  | Asn<br>195 |
| Cys   | Ser        | Gly  | Lys  | Ile<br>200 |      | Ile  | Ala  | Arg | Tyr<br>205 | Gly | Lys  | Val  | Phe  | Arg<br>210 |

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| Gly | Asn | Lys | Val | Lys<br>215 | Asn | Ala | Gln | Leu | Ala<br>220 | Gly | Ala | Lys      | Gly. | Val<br>225 |   |     |   |        |   |
|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|----------|------|------------|---|-----|---|--------|---|
| Ile | Leu | Tyr | Ser | Asp<br>230 | Pro | Ala | Asp | Tyr | Phe<br>235 | Ala | Pro | Gly,     | Val  | Lys<br>240 |   |     |   |        |   |
| Ser | Tyr | Pro | Asp | Gly<br>245 | Trp | Asn | Leu | Pro | Gly<br>250 | Gly | Gly | Val      | Gln  | Arg<br>255 |   |     |   | •      |   |
| Gly | Asn | Ile | Leu | Asn<br>260 | Leu | Asn | Gly | Ala | Gly<br>265 | Asp | Pro | Leu      | Thr  | Pro<br>270 |   |     |   |        |   |
| Gly | Tyr | Pro | Ala | Asn<br>275 | Glu | Tyr | Ala | Tyr | Arg<br>280 | Arg | Gly | Ile      | Ala  | Glu<br>285 |   |     |   |        |   |
| Ala | Val | Gly | Leu | Pro<br>290 | Ser | Ile | Pro | Val | His<br>295 | Pro | Ile | Gly<br>_ | Tyr  | Tyr<br>300 |   | · · |   | `\<br> | - |
| Asp | Ala | Gln | Lys | Leu<br>305 | Leu | Glu | Lys | Met | Gly<br>310 | Gly | Ser | Ala      | Pro  | Pro<br>315 |   | . 4 |   |        |   |
| Asp | Ser | Ser | Trp | Arg<br>320 | Gly | Ser | Leu | Lys | Val<br>325 | Pro | Tyr | Asn      | Val  | Gly<br>330 |   |     |   |        |   |
|     |     |     |     | 335        |     | Phe |     |     | 340        |     |     |          |      | 345        |   |     |   |        |   |
| ٠   |     |     |     | 350        |     | Val |     |     | 355        |     |     |          | ·    | 360        |   | ,   | , |        |   |
| ·.  |     |     |     | 365        | 4   | Glu |     |     | 370        |     |     |          |      | 375        |   |     |   |        |   |
|     |     |     |     | 380        |     | Val |     |     | 385        |     |     | -        |      | 390        | • |     |   |        |   |
|     |     | *   |     | 395        |     | Glu |     |     | 400        | •   |     |          |      | 405        |   |     |   |        |   |
|     |     |     |     | 410        |     | Pro |     |     | 415        |     | •   |          |      | 420        |   |     |   |        |   |
|     |     |     |     | 425        |     | Gly |     |     | 430        |     |     |          |      | 435        |   |     |   |        |   |
|     |     |     |     | 440        |     |     |     |     | 445        |     |     |          |      | 11e<br>450 |   | ,   |   |        |   |
|     |     |     |     | 455        |     |     |     |     | 460        |     |     |          |      | 465        |   |     |   |        |   |
| _   |     |     |     | 470        |     |     |     |     | 475        |     |     |          |      | 480        |   |     |   |        |   |
| Leu | Lys | Ser | Pro | Asp<br>485 |     | Gly | Phe | Glu | Gly<br>490 |     | Ser | Leu      | туг  | Glu<br>495 |   |     |   |        |   |

Die

| Ser          | Trp                  | Thr      | Lys   | Lys<br>500  | Ser <sub>.</sub> | Pro | Ser | Pro | 505        | Phe  | Ser | GLY      | Met | 510        |
|--------------|----------------------|----------|-------|-------------|------------------|-----|-----|-----|------------|------|-----|----------|-----|------------|
| Arg          | Ile                  | Ser      | Lys   | Leu<br>515  | Gly              | Ser | Gly | Asn | Asp<br>520 | Phe  | Glu | Val      | Phe | Phe<br>525 |
| Gln          | Arg                  | Leu      | Gly   | Ile<br>530  | Ala              | Ser | Gly | Arg | Ala<br>535 | Arg  | Tyr | Thir     | Lys | Asn<br>540 |
| Trp          | Glu                  | Thr      | Asn   | Lys<br>545  | Phe              | Ser | Gly | Tyr | Pro<br>550 | Leu  | Tyr | His      | Ser | Val<br>555 |
| Tyr          | Glu                  | Thr      | Tyr   | Glu<br>560  | Leu              | Val | Glu | Lys | Phe<br>565 | Tyr  | Asp | Pro      | Met | Phe<br>570 |
| Lys          | Tyr                  | His      | Leu   | Thr<br>575  |                  | Ala | Gln | Val | Arg<br>580 | Gly  | Gly | Met      | Val | Phe 585    |
| Glu          | Leu                  | Ala      | Asn   |             |                  | Val | Leu | Pro | Phe<br>595 | 'Asp | Суѕ | Arg      | Asp | Tyr<br>600 |
| Ala          | Val                  | Val      | Leu   | Arg<br>605  | Lys              | Tyr | Ala | Asp | Lys<br>610 | Ile  | Tyr | Ser      | Ile | Ser<br>615 |
| Met          | Lys                  | His      | Pro   | Gln<br>620  | Glu              | Met | Lys | Thr | Tyr<br>625 | Ser  | Val | Ser      | Phe | Asp<br>630 |
| Ser          | Leu                  | Phe      | Ser   | Ala<br>635  | Val              | Lys | Asn | Phe | Thr<br>640 | Glu  | Ile | Ala<br>- | Ser | Lys<br>645 |
| Phe          | Ser                  | Gl'u     | Arg   | Leu<br>650  | Gln              | Asp | Phe | Asp | Lys<br>655 | Ser  | Asn | Pro      | Ile | Val<br>660 |
| Leu          | Arg                  | Met<br>、 | Met   | Asn<br>665  | Asp              | Gln | Leu | Met | Phe<br>670 | Leu  | Glu | Arg      | Ala | Phe<br>675 |
| Ile          | Asp                  | Pro      | Leu   | Gly<br>.680 | Leu              | Pro | Asp | Arg | Pro<br>685 | Phe  | Tyr | Arg      | His | Val<br>690 |
| Ile          | Tyr                  | Ala      | Pro   | Ser<br>695  |                  | His | Asn | Lys | Tyr<br>700 | Ala  | Gly | Glu      | Ser | Phe<br>705 |
| Pro          | Gly                  | Ile      | Tyr   | Asp<br>710  | Åla              | Leu | Phe | Asp | 715        |      | Ser | Lys      | Val | Asp<br>720 |
| Pro          | Ser                  | Lys      | Ala   | Trp<br>725  |                  | Glu | Val | Lys | 730        |      | Ile | Tyr      | Val | Ala<br>735 |
| Ala          | Phe                  | Thr      | . Val | Gln<br>740  |                  | Ala | Ala | Glu | Thr<br>745 |      | Ser | Glu      | Val | Ala<br>750 |
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